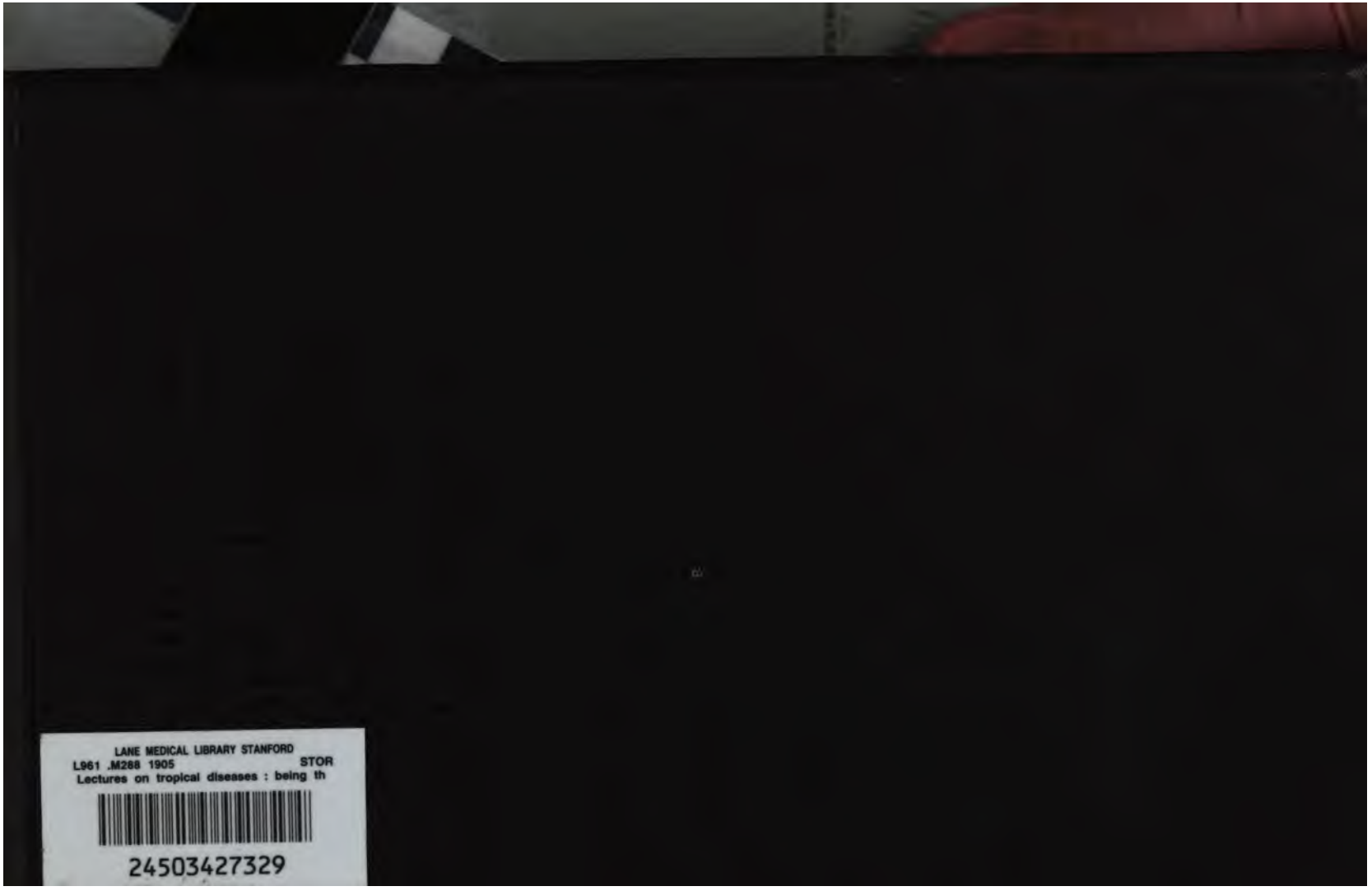

LECTURES ON
TROPICAL DISEASES

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TROPICAL DISEASES

BEING

The Lane Lectures

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BY

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LECTURES
ON
TROPICAL DISEASES.

I.

Principles Determining the Geographical Distribution of Tropical Diseases—Epiphytic disease: Ankylostomiasis.

My first duty is to thank the authorities of this College for the honour they have done me in selecting me as Lecturer on this occasion. It is no small honour, and it is one, I need hardly assure you, I highly appreciate.

While thanking you I would congratulate you, not on your choice of lecturer, but on your choice of subject. Considering the time and the place there could be no more appropriate theme than Tropical Medicine.

During the last few years tropical pathology has advanced by leaps and bounds, and probably at a greater rate than any other department of medicine. I was going to say every month—this may be exaggeration—but certainly every year brings with it some notable discovery, some new fact, some new disease, some fresh light on an old disease, or, it may be, some revolutionising idea pregnant with possibilities.

Thirty years ago tropical pathology as a distinct department of medicine could hardly be said to exist;

but within that short space of time how many important discoveries have been made! To mention but a few, I might point to the germ causes of leprosy, of cholera, of Mediterranean fever, of chyluria, of tropical splenomegaly, of tropical sore, and, most important of all, of malaria; it may be also of dysentery, of liver abscess, of sleeping sickness. Many hitherto unknown animal parasites, some exercising pernicious effects on their human hosts, have been dragged to light; and helminthology, until recently an insignificant, if not a despised, branch of pathology, has acquired an importance no longer to be ignored. The protozoa, formerly hardly mentioned in our text books, thanks mainly to research in tropical pathology, are gradually usurping the premier place hitherto held by the bacteria. Lastly, an entirely new and, especially from the standpoint of preventive medicine, a most important departure was inaugurated when it was found that insects and their congeners are instrumental, and in many instances are necessary agents, in the diffusion of a considerable section of human and animal disease. When the mosquito made her bow on the stage of pathology, and more especially when Ross demonstrated her *rôle* in malaria, a new and most important era in the science of medicine was inaugurated.

Manifestly the present is an appropriate time in which to discuss tropical medicine. Equally appropriate for this discussion is the building and the city in which we are assembled. Whether ye will it or no, America is bound to expand. I cannot pretend to say precisely what form this expansion is to take, whether it is to be in the shape of conquest, of colonisation, or merely of moral, intellectual, and commercial assimilation, or, in other words, as civilisation; but certain it is that one

way or another, and in the not very distant future, American influences will dominate a large and increasing proportion of the earth's surface. Seeing, however, that the greater part of the temperate regions of the globe are already fully occupied by kindred races and kindred civilisations, the latent energies of American expansion must find their vent and opportunity in the tropics, as indeed has already happened, and more especially in those lands whose shores are washed by the Pacific. For these lands this port of San Francisco is the natural jumping-off and dumping place. It takes little prescience to foretell that ere many years have passed thousands will annually leave your shores for tropic countries, and thousands will return to them from tropic exile. San Francisco will become a yet greater commercial centre, and will stand in this respect to the west of the American Continent very much in the same relationship as London used to stand to the west of Europe. The San Francisco of to-day is but a village as compared to the vast metropolis of the Pacific which it is her destiny to become.

The expansion of America tropicwards will undoubtedly bring in its train great material prosperity to this city. With this prosperity will come trials, duties, responsibilities. Not the least important of these are those having reference to disease and to the preservation of health in tropical countries.

The establishment of those admirable and fruitful research laboratories in the Philippines, the splendidly successful efforts made in Cuba to banish yellow fever, and the elaborate sanitary arrangements devised for the Panama Canal route, show that the Washington authorities thoroughly appreciate this. Doubtless the selection

of Tropical Medicine as the subject for these lectures was prompted by a similar appreciation on the part of the authorities of this College of what I might designate the situation.

When I sat down to write these lectures I made, by way of guide, a list of all the diseases, so far as known, that are more or less peculiar to the tropics. The contemplation of the length of the list I drew up soon convinced me that anything like a comprehensive or elaborate discussion of each and all of the diseases therein enumerated would be impossible in the few hours at my disposal.

Some sort of selection was necessary therefore. To help me to make this I placed myself, in imagination, in the position of one of my prospective San Francisco audience, and speculated as to what sort of information about tropical diseases I would like in such circumstances more especially to receive; what about these diseases would interest me most; and what would be most useful to me in my practice.

And so I concluded to speak to you, in the first place, about those general principles which determine the occurrence of diseases special to the tropics, and which are responsible for the peculiar distribution of tropical diseases. This subject I placed first in order, seeing that a knowledge of the principles to which I refer is a guide, not only to the intelligent study of the etiology of tropical diseases, but also to their diagnosis, to their prophylaxis, and to their treatment. Moreover, this knowledge is the surest guide to further discovery in the field of disease causes.

Next, while elucidating these principles, I concluded to describe some of the more recent advances in tropical

pathology—such, more especially, as have been effected since our student days.

Then I thought I would take up in a practical way the subject of those tropical diseases which you are most likely to encounter here in patients from abroad.

Next I considered it might be useful to speak in a comprehensive way about the diagnosis of these diseases; and, finally, to say something on the important subject of treatment.

Such in a general way is the task I have set myself. I know I shall fail to do justice to my subject; but if I succeed in interesting you in some of the tropical problems I shall touch upon, in giving you some hint that may help you in diagnosis and treatment, my long journey to San Francisco will not have been made in vain.

The various and manifold disease germs attacking man are not evenly and uniformly distributed over the globe. In this respect these germs resemble ordinary animals and plants. From a variety of causes some flourish better in one locality, some better in another locality. As in the case of ordinary animals and plants, atmospheric temperature, though not by any means the only, is a potent influence in determining distribution. Thus it is that in warm climates there are certain diseases peculiar to them, and others which, though not peculiar to warm climates, are specially prevalent there.

Although to this extent there is a parallelism in geographical distribution between the pathogenic germs and ordinary animals and plants, there is at the same time a striking contrast. And the contrast lies in this: that whereas, on the one hand, with the exception of man

and the domestic animals, the ordinary fauna and flora of the tropics are absolutely different from those of temperate climates ; on the other hand, the majority of the pathogenic fauna and flora of the tropics are the same as those of temperate climates.

I say the majority of the pathogenic fauna and flora ; for do we not find the tubercle bacillus everywhere, the typhoid bacillus everywhere, measles, smallpox, syphilis, whooping-cough, pneumonia, tetanus, and many other disease germs everywhere ? Certainly most diseases have a more or less universal distribution ; or, at all events, if through some accident of isolation or otherwise they may not occur in certain favoured spots, yet if introduced there, other circumstances being favourable, they are capable of flourishing and spreading regardless of atmospheric temperature or other climatic conditions.

I have said the majority of disease germs actually have, or are capable of, universal geographical and climatic range. The expression "majority" implies that there is a minority not so endowed. It is to this minority, or, rather, to a section of this minority, that the class of diseases designated "Tropical" belongs. There are some two or three diseases peculiar to temperate climates, limited almost to temperate climates—notably scarlet fever, typhus exanthematicus, and, in great measure, acute rheumatism. But by far the larger number of climatically restricted diseases are tropical diseases—that is to say, diseases absolutely confined to the tropics, and which cannot be introduced into colder climates ; or they are diseases which can be acquired only in the tropics, and which, although they may be introduced, do not spread in cold climates.

Thus, then, the parallelism between the distribution of ordinary plants and animals, and the distribution of the pathogenic plants and animals, is not complete; for whereas ordinary plants and animals have their distribution in every instance directly determined by climate, in the case of the pathogenic plants and animals only a few species are so affected, the majority being found, or being capable of flourishing, in all climates. To put it in another way I might say that as regards the tropics we have only plants and animals that are special and peculiar to those regions, whereas in the matter of diseases and disease germs we have nearly all the diseases of temperate climates with a considerable number of special and essentially tropical diseases superadded.

The explanation of this seeming biologic anomaly is the first point I would seek to impress on my audience. It involves a principle, perhaps the most important principle, in tropical pathology; a principle on the due apprehension of which our scientific grasp on tropical pathology and our power to extend the subject mainly depend.

Ordinary plants and animals are directly affected by the temperature of the medium in which they live. If this is suitable, other conditions being favourable, they live and multiply; if unsuitable, they die out. One plant requires a certain atmospheric temperature, climate and soil; another requires a different temperature, climate and soil. And as there is a vast variety and range in all of these conditions there is a corresponding variety in the plants and animals of different localities.

But in the case of the disease germs it is quite different. There is practically no variation in the climatic conditions nor in the soil in which they live; for their world, their climate and soil, is the human body with its practically

uniform temperature and its practically uniform pabulum. Regarded as a cultivating medium there is no difference between the juices and tissues of an Esquimaux and those of a Caucasian; or those of a negro; or of those of any given individual of any of these several races, whether that individual be living in the frigid, the temperate, or the torrid zones. Thus it comes about that a disease germ, say a tubercle bacillus, implanted into a human body at San Francisco will go on flourishing even if that body transfers itself to Panama; and thus it is that a malarial germ acquired in Panama will go on flourishing in the body of its host even if that host should come to the salubrious non-malarial shores of North California.

Not infrequently it happens that the presence of a disease germ, originally acquired in the tropics, is manifested for the first time, months or even years after tropical residence had ceased, and the patient is, as he supposes, safe in his native land. In London I frequently encounter cases of Blackwater Fever the germ of which had been acquired in tropical Africa. In a proportion of these cases the attack of Blackwater for which I saw the patient was his first attack of that disease. He may have left Africa several months before and have left it apparently in good health. That terrible African disease known as the Sleeping Sickness may remain latent for years, the natives say seven years. Some time ago I saw a case in which the characteristic symptoms did not show themselves until the patient had been over a year in England, and some eighteen months after the presumed date of infection. I know of another case in which the symptoms of Sleeping Sickness were not declared until the third year of residence in England, the lad, a negro, having enjoyed, I was informed, perfect health in the meantime.

Of course this capacity for prolonged latency is not peculiar to tropical disease germs; we have the same thing in such pandemic diseases as turbercle, leprosy, hydrophobia and others. But we are apt to overlook it in the case of tropical diseases, and to congratulate ourselves on having escaped tropical risks when we have escaped from the tropics. You may leave the place where you acquired the disease germ, but your blood, tissues and temperature remaining the same, the disease germ does not necessarily die out prematurely, nor quit you simply because you have changed latitude and longitude. The culture medium is not necessarily impaired as a culture medium by the change of climate and locality.

If, then, disease germs can thus thrive in the human body no matter where that body may be, how comes it, you will ask, that certain diseases are confined to warm climates? Why is it that we do not encounter all diseases everywhere?

Well, so far as I know, there are only two or three diseases that are, strictly speaking, confined to warm climates, that is to say that can neither be acquired in, nor be successfully imported into, nor thrive in colder climates. These two or three—I might call them non-exportable diseases—so like ordinary plants and animals in respect to their climatic delicacy, depend on germs, on plants, indeed, that live on the surface of the body and are therefore exposed like ordinary plants to climatic influences. As their climatic requirements include high atmospheric temperature and, in the case of one of them at least, moisture, they die off like a palm tree or other delicate tropical exotic when transferred to a cold or dry climate.

The diseases I allude to are the Central American skin disease called Pinta and that curious form of body ringworm, *Tinea imbricata*, which was first described by the medical officers of the United States Exploring Expedition to the South Pacific in 1841, under Commodore Wilkes. Some thirty years ago, while in South China, I paid some attention to this disease, proving its mycotic nature, and giving it the name it is now usually known by.

Tinea imbricata. (*After Koch.*)

When *Tinea imbricata* is fully developed the entire surface of the body is covered with a multitude of mutually complicating systems of concentrically-arranged rings of scales. This, to the ordinary individual extremely loathsome, but to the dermatological individual extremely handsome, skin disease, is widely diffused throughout the Pacific Islands and the Malay Archipelago, extending as far west as Burma

Fungus of *Tinea imbricata*.
(*From a photo by Dr. T. S. Kerr.*)

and as far north as the coast of South China. Recently some evidence has been forthcoming that it has appeared in Brazil. Not improbably, as communications with the endemic area multiply, it will show itself in the West Indies, Central America, and tropical Africa, or wherever the climatic conditions—a moist atmosphere and temperature between 80° and 90° Fahr.—are suitable to the fungus on which the morbid process depends. In many of the Pacific Islands a fourth, and in some of them one-half, or even a larger proportion of the natives are affected. Europeans are not exempt.

The trichophyton-like fungus which gives rise to the characteristic desquamation lies very superficially in the lower layers of the epidermis, which it detaches as it advances in its eccentric extension. After the first line of fungus has passed over some skin area a new epidermis forms and a fresh growth of the fungus starts to undermine it. This second line of fungus follows the first; the second ring is followed by a third, and so a never-ending series of parallel scaling rings is produced. This I might designate as the scheme of the disease. The eccentrically-spreading rings remind one of the ripples produced on the surface of a pond by a pebble falling on the calm surface. When the fungus spreads from many points, as owing to auto-infection is generally the case after a time, it is as if a shower of stones had fallen on the pond. Many systems of spreading rings are produced, which intersect each other in all directions and give rise to a pattern of extreme complexity, though of some regularity. The extension of the scaling area continues just so long as the state of the atmosphere is favourable. When the temperature mounts above 90° Fahr. or falls below 75° Fahr., or if the air becomes

very dry, the fungus dies, or at all events ceases to be active, and the disease spreads no longer on those already infected, or from man to man, and may even die out.

I have never seen the American equivalent of *Tinea imbricata*, namely, Pinta, but by all accounts in many respects it is the counterpart of the Pacific disease. Pinta occurs in special localities in the countries lying between Mexico in the north and Brazil to the south. It depends, apparently, on several varieties or species of fungi. As these fungi contain pigment, and as each species when in mass shows its special colour, blue, red, or black (and it is said white), Pinta results; and as the same individual may be affected by any or all of the varieties, in an extreme case the outcome is a skin mottled like that of a circus clown. So common was this disease in a certain Central American republic that the State could not afford to regard it as a bar to military service; the subjects of Pinta had to serve with the rest. A concession was made, however, in the interests of the more cleanly and non-infected, the victims of the painted skin disease were collected into special regiments known as "pintados."

The geographical limitation of diseases such as the foregoing, and perhaps of several other epiphytic tropical skin diseases not yet properly defined, admits of easy explanation. So, likewise, do the geographical limitations of certain tropical diseases produced by such ectozoa as the chigger, the screw-worm, and other anthropophagous larvæ and annelids. Not so, however, the geographical limitations of the other and vast majority of tropical diseases. In the case of the latter another and much more complex explanation must be sought for.

Observe, in the first place, that although all tropical diseases, other than the epiphytic and ectozoic diseases just alluded to, can be exported in the sense that once their germs are implanted they can be carried to and can run their course in any climate, yet it is only in warm climates that they can be acquired or can spread.

A manifest inference from this is that although climate does not affect the germ once successfully implanted, yet there must be something in climate that affects the germ before it is acquired—that is to say, during its passage from the sick to the sound. In this circumstance lies the key to the successful study of the etiology of tropical diseases, and also to their successful prophylaxis. When the student has thoroughly grasped this idea and all that it implies, he has made the first and most important step in the science and practice of tropical medicine.

In studying the natural history of the majority of the disease germs peculiar to warm climates we find that climate exercises its influence in one of several ways. These ways I propose to consider and to illustrate somewhat in detail:—

1st. The germ after it has left the body of a human host has to undergo certain developmental changes for which a warm medium is required—warm earth or warm water—before it is fitted to re-enter another human host.

2nd. After leaving the body and being deposited in earth or water, the germ may have to undergo developmental changes in the body of some tropical animal intermediary before it can effectively re-enter another human host.

3rd. The germ may not be able to escape spontaneously from its original human host, but has to depend on the services of some tropical animal to abstract it therefrom, and perhaps to re-implant it into its next human host.

4th. This abstracting and implanting agency may be required not only for these purposes, but also to serve as a medium in which the immature germ may undergo developmental changes necessary for enabling it to re-enter on parasitic life in man.

5th. Certain tropical toxæmias whose toxines are produced outside the human body depend for their virus on germs acting on certain media, for which action high temperature is necessary.

In the class of diseases I propose to consider first, the germ, or, rather, young or ovum of the germ, having left the human body in a form incapable of immediate re-entry, has to pass through certain evolutionary changes before development has attained such a point that the organism in question is able to resume parasitic life. Now, if for this process of development a sustained high temperature be necessary, the germ, and of course the disease for which it is responsible, can be acquired only where this high temperature is available—that is to say, in tropical conditions.

The disease that used to be known as coolie anæmia, tropical anæmia, sometimes, though very erroneously, as beri-beri, is an illustration in point. This often very grave condition is now known to depend on the presence
1 the intestinal canal of a certain hook-worm—the
lostomum duodenale. Hence the modern name for
ase—Ankylostomiasis.

Ankylostomum duodenale—Male: highly magnified.
(*Photo by Dr. T. S. Kerr.*)

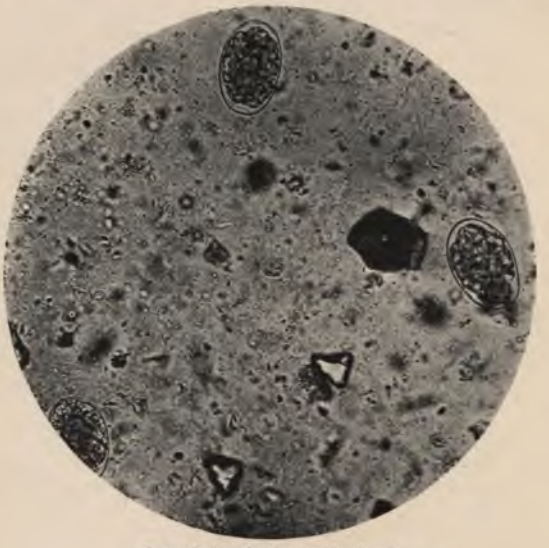
The worm, so far as size is concerned, is a very insignificant one, but in consequence of the local irritation and accompanying dyspepsia it gives rise to, of the direct loss of blood from its leech-like habits, and of a peculiar hæmolytic toxin it is said to secrete, this insignificant innocent-looking parasite brings about a state of anæmia in its host, always of a debilitating character, and sometimes so profound as to lead more or less directly to serious invaliding or it may be to death.

Ankylostomum duodenale—Female: highly magnified.
(*Photo by Dr. T. S. Kerr.*)

Seeing that it gives rise to conditions so serious, and seeing that it is a very common parasite in the tropics, the anky-

lostomum, though merely a worm, is a disease germ of the first importance and well worth serious consideration and study.

The ankylostome, a little thread-like organism scarce half an inch in length, is oviparous. It lives in the small intestine and lays its eggs into the contents of the bowel, whence they emerge in the fæces. If the eggs thus



Ova of *Ankylostomum duodenale*
(Photo by Mr. R. Muir.)

escaped are kept warm in a suitable medium, preferably damp earth, they hatch out, and a microscopic living, and at first very active, embryo is set free. It rapidly acquires organs of digestion, and after casting its skin several times and undergoing other evolutionary changes, is ready to re-enter a human host.

Thanks to the brilliant researches of Loos, we now know precisely how this re-entry is often, if not invari-

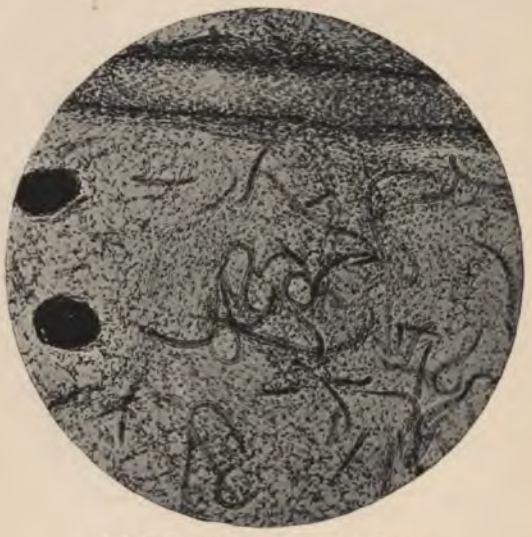
ably, effected. Formerly it was asserted, and believed, that the young ankylostome entered the human alimentary canal by being swallowed in dirty water, or by being transferred on earth-soiled hands or dishes to the mouth and so to the stomach. Loos has shown that this idea is not always correct, perhaps is wrong. Ankylostome embryos so transferred to the human stomach are di-

Embryo of *Ankylostomum duodenale.*
(Photo by Mr. R. Muir.)

gested, he contends, just as an oyster would be digested. The process of re-entry is a far more complicated one than that of simple ingestion; it involves a stage of preparation by which the immature worm is enabled to resist the action of the digestive juices.

Loos has shown that when the necessary developmental changes of the exogenous phase of the embryo

have been completed, on a suitable opportunity offering the little worm penetrates the skin, generally that of the feet or legs, of the coolies or others working in, or passing through, or otherwise being brought in contact with contaminated earth in which ankylostome ova had been previously deposited. Given this opportunity the embryo ankylostome enters the skin through some follicle and



Ankylostome embryos beneath epidermis.
(*Photo by Mr. R. Muir.*)

thence passes into a blood vessel, and so, *via* the heart and pulmonary artery, to the lungs. Arrived here it leaves the blood vessels, and after undergoing further changes, those that enable it to resist the gastric fluid, enters an air vesicle, thence passes to a bronchus, and so by way of the trachea, œsophagus and stomach, ultimately attains its permanent abiding place—the small intestine. Arrived there, sexual characters are assumed

and reproduction commences, the resulting ova falling into the contents of the gut.

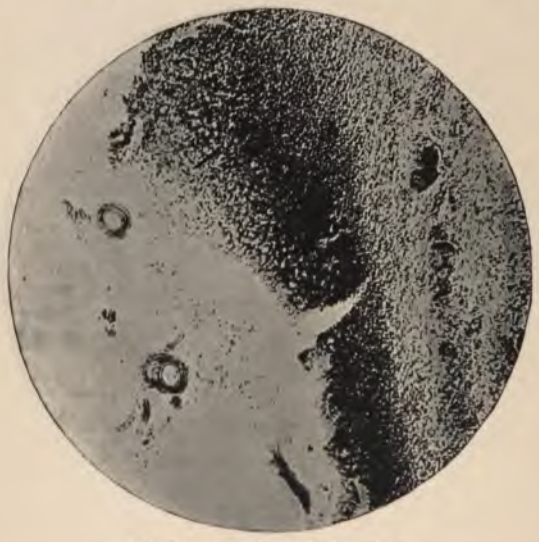
From this brief sketch of the history of the ankylostome it is evident that the most critical period of its life, that in which it is most exposed to danger, that in which there is the greatest liability to destruction, or at least suppression, by the presence of unfavourable conditions

Ankylostome embryos in vein.
(*Photo by Mr. R. Muir.*)

or the absence of favourable conditions, is that during which it is passing from one human host to another. Of these conditions temperature is an important one. Should the temperature of the medium in which the young parasite is lying fall during this period below a certain point, as of course it must under ordinary conditions in temperate climates, the necessary developmental changes are suspended or are never commenced,

and the worm and the disease it gives rise to do not spread.

Loos's discoveries have thrown important light not only on the way in which a special form of tropical anæmia—ankylostoma anæmia—is acquired; but they have illuminated another tropical disease, one hitherto misunderstood, and which, though comparatively trifling



Ankylostome embryos in bronchus.
(Photo by Mr. R. Muir.)

in itself, has a certain importance, inasmuch as it serves, when it appears on a plantation or elsewhere, as a warning that the ankylostome is about. I allude to what is known in some places as "Coolie itch," in other places as "Ground itch."

This is a sort of papulo-pustular dermatitis, generally attacking the feet and legs, but at times other surfaces as well. From the scratching it induces, and the secondary

infections—such as phagedena—that may be superposed, serious lesions may ensue. On many plantations it is very common and is itself the cause of a good deal of invalidism among the coolies, and therefore of financial loss to the planter. It had, indeed, been observed that an attack of Coolie itch was frequently the prelude to anæmia. But although Bentley, working in Assam, had

Ankylostome embryos in stomach.
(*Photo by Mr. R. Muir.*)

demonstrated the embryo ankylostome in the lesions of Coolie itch, no one suspected, until Loos indicated the route by which the ankylostome effects its entry into the human body, that Coolie itch was but a phase of Tropical anæmia, of Ankylostomiasis; that the papules and pustules were but an incident in a disease with graver issues; in other words, that they were produced by the ankylostome in effecting its entrance through the skin.

Having mentioned Coolie itch, I am tempted to tell you of something which, although it has no very direct bearing on my argument, is interesting as showing how near a man may get to an important discovery and yet miss it, and also as illustrating the not uncommon fact that correct treatment and correct prophylaxis may be based on wrong theory.

A planter from Trinidad, West Indies, told me some time ago that he was at one time seriously inconvenienced by Coolie itch among his field hands. He remarked that the attack of Coolie itch was often followed by profound anæmia; and he also remarked that the skin disease and the anæmia occurred only, or principally, among the coolies who either passed through or who worked in certain fields. He argued that in these fields there were certain germs that, coming in contact with the legs and feet of the coolies, produced the dermatitis and, on subsequently entering the body, the specific anæmia. He knew nothing about the ankylostome; the observation was made long before Loos's discovery.

The planter had some knowledge of bacteriology, and he, like many others, thought that the germ in question was a bacterium, and that by means of some antiseptic and protective procedure he could either kill the germ or prevent its access to the skin. In casting about for means to effect this he bethought him of a practice he had seen in operation in a certain part of Germany during one of the annual pilgrimages he made to that country in search of health. In that particular part of Germany geese are raised in large numbers. The goose market is a long way from many of the goose farms, so that the birds when ready for sale have to be driven for many miles over the hard roads. To enable their

feet to stand the journey, the farmer provides each of his fat birds with a pair of close-fitting antiseptic socks and sandals. These he fits on in this wise. He fills a shallow trough with tar, and through this trough he drives his geese on to a piece of ground covered with a layer of fine sand. The tar sticks to their feet and the sand to the tar; the birds are shod for the road. Thus provided, they perform the long journey without injury.

Acting on this hint the planter made his coolies, on their way to their work in the morning, dip their feet and legs in a bucket of Barbadoes tar and then walk across a layer of sawdust or sand. The result was excellent. Coolie itch and coolie anæmia almost disappeared from the plantation. This easily applied, inexpensive, and thoroughly rational prophylactic measure I commend to your consideration.

I frequently meet with cases of Ankylostomiasis in England, principally in natives of warm climates, but occasionally also in Englishmen from the tropics, who have brought home the disease with them. These cases do not, as a rule, serve as foci for the infection of others; our climate, under ordinary circumstances, is too cold for the hatching out of the embryo and for its life during the free non-parasitic stage. But even in England, if the necessary tropical conditions are reproduced by artificial means, Ankylostomiasis will spread just as readily as it spreads under natural conditions in warmer latitudes. Recent experiences illustrate this very well, and show that as regards the particular category of tropical diseases to which Ankylostomiasis belongs, it is temperature that is the principal factor that determines their extension.

In the county of Cornwall there are certain tin mines that have attained a great depth. In these deep mines the temperature of the lower workings is necessarily very high. Cornish miners wander all over the world in pursuit of their calling. Some of them return to the old country and to the old workings. In the case of the particular mines I refer to, the ankylostomum had been introduced by some of these repatriated miners, and being introduced, it spread apace in the tropical temperature of the lower workings. For a long time all sorts of theories were put forward about the cause of the epidemic of anæmia that had broken out among the miners. Hundreds were affected; there was much invaliding and some deaths. Ultimately the true cause of the anæmia was discovered by Prof. Haldane, and appropriate treatment and prophylaxis being instituted, the anæmia and its cause is disappearing from these Cornish mines. But now another problem has cropped up. Ankylostomiasis having been introduced into the mining community of Great Britain, may it not appear in other mines, the coal mines, for example, mines which are in some places carried to a great depth, and are proportionately warm and are not always in perfect sanitary condition? This, considering the huge mining population of the country, would be a calamity indeed. In Westphalia, and in certain other coal mining districts in the continent of Europe, such epidemics have occurred and are still in progress. They have proved a serious tax on the industry. The labours of Wardell Stiles and others in your own country have brought to light the wide prevalence of Ankylostomiasis in certain places and institutions in this country, as well as the interesting fact that America has a variety of ankylostome peculiar to

itself. You have, therefore, a special interest in this subject.

Let me give you one word of advice in connection with Ankylostomiasis. It is this—whenever you encounter a case of anæmia, the explanation of which is not apparent, or which has resisted the usual methods of treatment, think of Ankylostomiasis and examine the stools microscopically; or, if not familiar with such things yourself, have them examined by someone who is. I could narrate many instances showing the importance of this. A medical man once sent me some slides of fæces, requesting an opinion as to the nature of the ova they contained. The patient was a soldier who had been invalided home from the West Indies. He had been for months in hospital, and, not improving, had been discharged from the hospital and the Army as being the subject of a pernicious anæmia. The ova in the stools were ankylostoma ova. The diagnosis and appropriate treatment soon cured the pernicious anæmia.

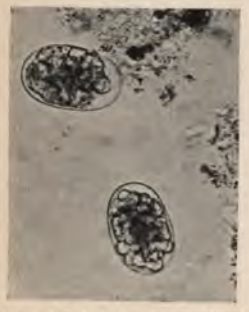
It is only quite recently that the verminous nature of the coolie anæmia of the West and East Indies has been recognised. Better late than never; but it is sad to reflect on the huge volume of suffering and loss of life, not to mention the loss of labour, which this delay in utilising a discovery made many years ago has entailed, and for that matter still entails, especially, but not exclusively, on tropical mankind.

A word in conclusion on the diagnosis, treatment, and prophylaxis of Ankylostomiasis. Our knowledge of the etiology of the disease is an efficient guide.

The first step towards diagnosis is to suspect. An anæmia in the tropics or in someone from the tropics, in the absence of the usual and more familiar causes of that

condition, should suggest a microscopical examination of the fæces for ova of the ankylostomum. If the ova are found the probabilities are that the case is one of ankylostoma anæmia, and a suitable treatment should be instituted.

We have two fairly efficient remedies—filix mas and thymol. Of the two the latter is the drug most in favour at present. Filix mas is given in the usual way and in the usual doses as for tape worms. In giving thymol the patient should be prepared in the same way as for filix mas by twenty-four hours of comparative starvation, and one to two doses of some saline aperient. The thymol should then be given in cachet or in suspension—never in alcoholic solution—in doses of thirty grains every hour for three or four times, the last dose being followed by a smart purge. This poisons and expels most of the worms. If after a week, on microscopic examination of the stools, ova are still found to be present the thymol must be repeated. Until the thymol has been got rid of by the action of the purgative the patient should abstain from alcoholic drink of all kinds and keep his bed. Alcohol is a solvent of thymol which, if absorbed in considerable quantities, may exercise toxic effects on the patient as well as on the worm.



Ova of *Ankylostomum duodenale*.
(*Photo by Mr. R. Muir.*)

Prophylaxis consists in care in disposal of such excreta as may contain ova of the ankylostome—no easy matter in the case of indifferent and ignorant coolies—and the protection, by some such means as I have already

referred to, of food and drink as well as of hands, legs, and feet, from contamination with material likely to contain embryos. As moisture is necessary for the well-being of the free embryo it is evident that, where feasible, the soil in the neighbourhood of houses and the workings in mines should be kept dry as well as protected from fæcal pollution.

In all tropical countries intestinal parasites are exceedingly common. A large proportion of the natives in most places carry about with them a stock of *Ascaris lumbricoides*, *Tricocephalus dispar*, and very often a few ankylostomes; but besides these we occasionally meet with two minute nematodes—*Strongylus stercoralis* and *Strongylus subtilis*. Though interesting from the helminthological standpoint, and in their life histories resembling the ankylostome, these two minute worms have very slight, if any, pathological significance, and as we know very little about their life histories they hardly call for more than mention.

II.

Dracontiasis: Endemic Hæmoptysis.

The extra-corporeal life of the next group of germs or parasites of which I shall speak is more complicated than that of *Ankylostomum duodenale*, described in my first lecture.

Just as in the case of the ankylostomum, the ova or embryos leave the human body in the excreta, or it may be in the secretions, or through some skin lesion; but unlike ankylostomum, the first start in life is made in the water, not in the soil. The embryo is passed into, or, if not already free, is hatched out in the water, where it swims about until a happy chance enables it to enter a suitable animal intermediary in which to undergo further and necessary developmental change. When these preliminary changes are completed the still immature parasite escapes from its intermediary, and then in water, or encysted on some aquatic plant or animal, finds its way back to man.

The intermediary being a tropical species, the parasite also is necessarily tropical; and therefore the disease to which it gives rise can be acquired only in the tropics.

It is quite possible that some of the protozoa—for example that known as Leishman's body—may have some such life history; but as yet, so far as this dangerous organism is concerned, our knowledge is too limited to justify anything like a positive statement on this important point. But as regards certain trematodes and

nematodes, either direct observation, or analogy, warrants us in concluding that substantially the route described is that by which they pass from human host to human host.

I shall select, as illustrating this method of infection, three tropical parasites each of which may, and often does, give rise to grave disease.

I. Guinea worm.
II. *Paragonimus westermanni.*
III. *Schistosomum hæmatobium.*

Of the three perhaps the most curious and interesting is the Guinea-worm—*Dracunculus medinensis.* It occurs in India, Persia, Arabia, Africa, but not, at least at the present day so far as I am aware, in America or in Asia anywhere east of India. In many parts both of India and of Africa it is exceedingly common, especially so at particular times of the year. Large numbers of the natives may be affected, and not infrequently European visitors are victimised.

You are not likely to see Guinea-worm cases in America, but for many of the tropical possessions of Great Britain Dracontiasis, as it is called, is quite an important disease. Every year I see several cases in London. The patients are mostly lascars or native sailors from India, but now and again I see the disease in travellers or soldiers from tropical Africa. In many parts of West Africa it is a positive tax on the military departments of the various colonies. A soldier with a Guinea-worm in his leg cannot march, very often he is seriously ill, and it may be three or four months before he is of any use for campaigning. And when in a body of soldiers you get one case you are nearly sure to have many cases, for all

have most probably been exposed to the same chances of infection.

Thus in September last an outbreak of Guinea-worm occurred among the black troops stationed at Old Calabar. The disease was acquired during an expedition in the hinterland some twelve months before. At first the cases were few, but they soon rapidly increased in number, so that on some mornings upwards of sixty soldiers were on the sick-list suffering from Guinea-worm. So serious was the outbreak that, owing solely to this event, a company of soldiers had to be requisitioned from Lagos to assist in carrying through the military operations which had become seriously hampered by the big sick-list. In this epidemic 161 cases, including four European officers, occurred, that is 15 per cent. of the force employed.

The Guinea-worm at maturity is a long, white, cylindrical organism some two or three feet in length and about as thick as fine whipcord. She (the female alone is known) is of uniform thickness throughout, unless for about an inch or thereby where she tapers slightly to the abruptly rounded-off head and to the hook-terminated tail. She lies irregularly disposed in the connective tissue between the muscles or under the skin. She has a good knowledge of anatomy, for when at maturity she moves down to the leg or foot, as she generally does, she never wounds the blood-vessels or nerves, and rarely strays into the joints. In due course, when ovulation is completed and her embryos are ready for temporary independent life, she drills a little hole in the derma, but does not penetrate the epidermis. Over this hole a small blister or bulla forms—perhaps half an inch in diameter. By and by the bulla bursts, or is ruptured, disclosing a

superficial circular erosion in the centre of which may be seen the minute hole leading to the worm, or from which half an inch or more of the head of the worm may be seen protruding.

The appearance of a Guinea-worm at the surface of the body is sometimes heralded by a rise of temperature and an urticarial eruption, a phenomenon in harmony with similar evidences of absorption of some form of toxine elaborated by several of the larger animal parasites. The same kind of constitutional disturbance may take place from the absorption of hydatid fluid, in infection with round worm, tape worm, etc.

Transverse Section of a Guinea-worm.
(*After Leuckart.*)

If at the time of her appearance at the surface of the body you manage to procure an uninjured Guinea-worm and dissect her, you will find that from head to tail she is little more than one long tube packed with young. To accommodate the millions of long-tailed embryos nearly every organ of her body has been more or less sacrificed. The uterus itself is reduced to an exceedingly delicate non-muscular tube, its functions as a contractile organ having been delegated to the stout musculo-cutaneous integument which constitutes the outer skeleton of the worm. Even the alimentary canal is but a mere thread.

Although thus devoting herself practically entirely to

reproduction, the Guinea-worm is nevertheless at this stage in a grave obstetrical dilemma. In the process of uterine expansion her vagina has become obliterated. Moreover, owing to her position at the surface of the body, if by any means she should succeed in expelling her young most probably they would perish from want of their proper element, which, as I shall presently show, is water.

Here, then, we have an organism packed with an enormous brood of water-demanding embryos, without a contractile uterus, without a vagina, and far away from the element her young require. How does she manage to launch her brood so that they may obtain a chance of life and so continue their species? By a very simple and easily-performed experiment you may learn in what way Nature cuts this Gordian knot and gets over what, to all appearance, are insuperable difficulties.

Perhaps some of my audience may think I am wasting time over these apparently trivial helminthological details. I do not agree with this opinion. These parasites, as I have shown, are in themselves of great practical importance. Moreover, by the contemplation and study of their habits, of their biological requirements, of their difficulties and contrivances, we are sometimes led by suggestion and analogy to a clearer and better understanding of the more minute, more difficult to observe and, from the medical and practical point of view, perhaps more important disease germs. At least I have found it so. The same laws, the same logic apply to big and little parasites alike; they are more easily perceived, more readily grasped and studied in the case of the larger organisms. Thus the study of helminthology is not only of direct practical value, but it is an admirable introduc-

tion to the still more complicated and obscure problems of protozoology and bacteriology.

To return to our experiment. Let us suppose a Guinea-worm has broken cover about the dorsum of a patient's foot. As a rule, all we see is a small circular erosion with a minute hole at its centre. Now place the patient's foot in a good light, and in a position favourable to close observation. Fill a sponge with cold water and, squeezing the sponge gently, get a trickle of water to fall on the foot some distance—say a couple of inches—from the little sore. The water need not, and for our purpose should not, touch the sore.

Meanwhile watch carefully the little hole. In less than a minute, the cold water trickling on to the foot the while, there will suddenly well up from the little hole and overflow the sore a few drops of a milky looking fluid. In ten or twelve seconds this flow will cease, and it cannot be reinduced until after some hours when a fresh application of cold water will again provoke it.

Take up in a watch glass some of the milky fluid and place it under a low power—an inch objective—of the microscope. It is a mass of embryo Guinea-worms, each worm bent on itself with its long slender tail sticking out at a tangent from the ring in which the body is disposed. There is very little movement beyond now and again a wag of the tail. Now add some water to the watch glass. In a few seconds the little worms extend themselves and begin to swim about, at first slowly, then with increasing vigour, until finally the preparation is a seething mass of wriggling worms—a most remarkable sight. Manifestly the young Guinea-worms are in their proper element. They will live thus for eight or ten days, some of them, especially in muddy water, even longer.

Evidently we have assisted at the parturition of a Guinea-worm, and at the introduction of her young to their future career.

But, you may ask, how has the worm managed to get over the difficulty of the absence of a vagina which had become obliterated, and the absence of contractile elements in her uterus, which was necessitated in order

Embryo Guinea-worms.
(From a photogram by Mr. H. B. Bristow.)

to accommodate the prodigious swarm of embryos with which she is packed from head to tail?

If you have patience and visit your Guinea-worm daily, and douche the patient's foot daily, keeping the worm from injury in the intervals by covering the sore with some simple non-poisonous dressing, very likely you will get your curiosity gratified, and will witness a display of obstetric surgery not to be beaten even in the most advanced clinics.

Sooner or later, at one of your daily visits, on removing the dressing you will find that the worm herself has partly emerged from her hole, half an inch or even more of her head protruding. Now repeat the douching and watch the head carefully. Presently a beautiful delicate and pellucid tube is slowly projected from her mouth to the extent of three quarters of an inch or thereby. At first clear, the contents of the tube rapidly become milky, evidently from milky material being forced into it from behind. The little tube now becomes very tense. Suddenly it ruptures, collapses, and the milky fluid containing the embryos is spilt over the sore and surrounding skin. A wonderful thing this. Parturition has been effected in response, be it observed, not to a stimulus applied directly to the worm herself, but to a stimulus—the cold water—applied to the skin of her host with whom she has no organised connection. Somehow this stimulus has induced contraction of the musculo-cutaneous coat of the worm, which thus comes to function as a uterus by forcing the uterine tube with its contents through the mouth of the worm.

When the prolapsed uterus ruptures, the protruded and now collapsed portion shrivels up into a mere thread, the rapid drying of which effectually and firmly closes the womb for the time being. But on re-application of the stimulus of the cold douche some hours later a fresh portion of uterine tube is protruded, ruptures and collapses, once more securing the discharge of another batch of embryos. And so the process goes on, until inch by inch the entire uterus is expelled and parturition is concluded.

The process takes from about a fortnight to three weeks to complete. When this, her sole object in life, is

attained, the worm dies, and is expelled or more often is pulled out bit by bit, or entire and with or without suppuration.

Strange midwifery this; full of meaning and purpose if we but interpret it aright. Let us see if we can.

In nine cases out of ten the Guinea-worm presents in a foot or leg. There is reason and significance in this. The foot and leg are just those parts of a Negro's or Indian's body that are most frequently brought into contact with water—that is to say, the element required by the embryo Guinea-worm in its first step in extra-corporeal existence. As it would be mere waste of life were the parent worm to expel her young where there is no likelihood of their finding water, she usually travels to the lower part of the lower extremities and there waits patiently, prepared to respond at once to the signal supplied by the immersion of the foot, that her opportunity has arrived. This signal given, her young are promptly spewed, as it were, from her mouth and securely launched into their proper element.

This sounds like fiction. But it is not fiction; it is absolutely true. I have over and over again witnessed this marvellous display of what, for want of a better name, we term instinct, and I have often shown these things to our students at the London School of Tropical Medicine.

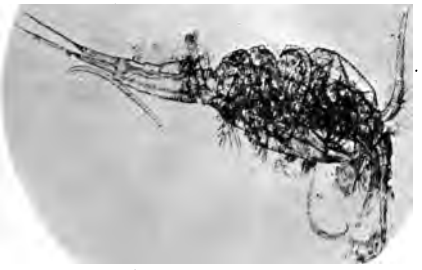
I believe the worm, long before she is ready to expel her young, comes to the feet and legs because, if I may use the expression in speaking of so humble and brainless an organism, she knows that these are the parts oftenest in contact with water. She is attracted by the water. I have reasons for this belief. In the few cases of Guinea-worm I have seen in the shoe and stocking wearing, but

bath loving, European, in a large proportion of them the parasite has presented somewhere on the surface of the trunk, scrotum or thighs, parts just as frequently in their case in contact with water as are the feet and legs. In the case of the Bheesties or water carriers of India, who carry the water in leaking skins slung over their backs, when they are attacked by Guinea-worm the parasite presents very frequently on the back—that is to say, in the part most frequently in contact with water. The Guinea-worm knows this.

There can, I consider, be no question as to the influence of the presence of water in determining the region of the body selected by the Guinea-worm from which to discharge her young. I suggest that this is brought about by the frequent contact of this region with water, a circumstance of which, as proved by the experiment I have just narrated, the parasite evidently takes cognizance. It may be that the water attracts and draws her. On the other hand it is quite possible that the parasite appears at water-bathed parts because she has developed in these parts, having entered the body there originally. The point, an interesting one, has not been settled. There is some evidence indeed that the latter conjecture may be correct. Thus the four European officers in the expedition in West Africa, to whom I have already alluded as having been victimised by Guinea-worm, throughout the whole of the campaign drank only filtered or boiled water, and therefore were not likely to have swallowed young Guinea-worms and so become infected by the mouth, but they did bathe frequently in the dirty water of the country, and might have been infected in this way through the skin.

Let us now follow the career of the young Guinea-worm

and endeavour to ascertain why the parent worm has been at such pains to get her brood into the water. We will try another experiment. Procure some fresh-water cyclops from a weedy pool and place them in a watch glass, along with the young Guinea-worms and a liberal supply of water. Leave them together overnight. Next morning examine the cyclops one by one with a low power of the microscope. In nearly every instance you will find one, two, three, or it may be a dozen young Guinea-worms slowly coiling and uncoiling themselves in the body cavities of the little crustaceans. They have effected an entrance by boring their way through the delicate membrane that unites the plates of the ecto-skeleton. You may even see them engaged on this operation, which the cyclops evidently resents but is powerless to prevent. They deliberately select cyclops; for if there are any other species of crustacean in the water, as is likely, daphnia for example, these they will not enter. Manifestly some species of cyclops is the proper intermediary of the Guinea-worm.



Guinea-worm embryos in body cavity of cyclops; two embryos lying outside the cyclops have been expressed in making the preparation.
(*From a photograph by Mr. Andrew Pringle.*)

Keep a stock of infected cyclops in a warm room and from day to day dissect one, either by tearing it up with needles or by crushing it under a cover glass. You will,

in the course of a few days or weeks, be able to ascertain that the worms undergo a process of development during which they drop their tails, cast their skins several times, become greatly increased in size, and ultimately obtain well-developed alimentary systems.

So far the development of the guinea-worm has been traced. The remainder of its life history is a blank. It has been conjectured, as I have hinted, that after completing the necessary developmental changes in cyclops the parasite is swallowed in drinking water while still in the body of the crustacean or, it may be, after it has escaped from this intermediary; or that it may obtain access to the human tissues in the same way that the ankylostomum does, namely, by boring its way through the skin, being picked up by the human victim while wading or bathing in infected waters. What the male worm may be like, or where or when impregnation is effected, has still to be ascertained.

Evidence is accumulating that the life-span of this parasite is just about one year. The fact that in certain places there is an annually recurring Guinea-worm season points to this conclusion. Of similar significance is the fact that two or more fellow travellers in a Guinea-worm district have subsequently and simultaneously developed the usual evidences of a Guinea-worm infection a year from the date of their visit to the endemic locality.

Some time ago I was asked to see, in consultation, a gentleman who had Guinea-worms presenting in both his thighs—two on one side, one on the other side. He told me he had just returned from India, where during the previous three months he had been on a shooting expedition, and where, according to his view, he had acquired the parasites. I told him that this view was erroneous,

seeing that the Guinea-worm took a year to mature. On further inquiry I learned that about a year before I saw him he had visited Lake Rudolf, in British East Africa, returning to England viâ the Nile. Undoubtedly, it was during this trip, and not during his subsequent visit to India, that he had become infected. Two or three days after I saw this gentleman I was consulted by another sportsman traveller, also about a Guinea-worm, which, in his case, was presenting in the right axilla. I asked him where he had been a year before. He told me at Lake Rudolf, and that he had come home by the Nile. "Strange," I said, "I have only quite recently seen another patient, suffering from Guinea-worm, who also had visited Lake Rudolf a year ago, and had come down the Nile." "What is his name?" he asked. I told him. "Why," he said, "he was my companion." Undoubtedly these two fellow travellers had picked up their Guinea-worms at the same time, or about the same time. This little narrative proves that the period I mention, one year, is about the limit of the life-span of *Dracunculus medinensis*. Manifestly this year-long life-span has reference to, is an adaptation to, the habits of its special kind of cyclops intermediary host, which, in turn, depend on special hydraulic and thermic conditions recurring annually in the endemic area.

I say special kind of cyclops, and perhaps additional intermediary host; and for this reason: Were the presence of cyclops the only condition determining the presence of Guinea-worm, then Guinea-worm would not be nearly so limited in its distribution as fortunately it is. Even in the endemic districts it is acquired only in certain places from certain wells or pools of water where, undoubtedly, some peculiar condition, perhaps some

peculiarly favourable species of cyclops, occurs. Not improbably after quitting cyclops the larval Guinea-worm has to enter yet another intermediary, possibly for sexual purposes, before it is fitted to invade the tissues of man. This blank in our knowledge of the life history of the Guinea-worm demands further study. Anyone desirous of undertaking this very interesting and important piece of research must visit the endemic districts and set himself to work out the fauna of the Guinea-worm pools which, usually, are very well known to the natives.

The Guinea-worm embryo has a long and danger-beset road to travel before it arrives at maturity. The prodigious number of its young indicates this. Of the millions that set out on the journey, only one or two ever reach the goal of maternity. The chances of any given embryo of any parasite, or other animal for that matter, arriving at maturity is in rough proportion to the fertility of the species. Nature meets difficulties of this description by multiplying proportionately the numbers of those that face them; millions perish, one succeeds.

The habits of the Guinea-worm have a practical, as well as a scientific, interest. Their proper appreciation is, or should be, our guide in treatment. If they are disregarded, and if the Guinea-worm is maltreated, she may prove a really dangerous parasite and give rise to lesions of a serious, sometimes of a grave or permanent character. If, as is too often the case, rude attempts at extraction are made before the worm has finished the emptying of her uterus, she will resist with all her might, and, clinging to the tissues by means of the hook at her caudal end, snap across rather than suffer extraction. Then the trouble begins. Her myriad brood, escaping

from the severed body, get into the tissues of the host and cause a considerable amount of irritation and much swelling. Micro-organisms of suppuration finding their way along the track in which the broken-off portion of worm had lain, and entering the area of irritation, produce violent inflammation, abscess, and sloughing. Much suffering ensues, and weeks, it may be months, elapse before the patient is able to get about again.

The proper treatment, therefore, that which is indicated by our knowledge of the habits of the Guinea-worm and endorsed by experience, is either to leave her alone, protecting her from injury; or to excise her bodily; or to kill her at once, taking care not to rupture her body deep down in the tissues.

From an Old Print, showing Guinea-worms and Loa being extracted by the Natives of West Africa.

She can be killed easily by injecting her through her mouth, using a hypodermic syringe for the purpose, with one in a thousand solution of bichloride of mercury. This not only kills her, but renders her and the track she lies in aseptic. She can then, usually after a day or two, be slowly wound out round a piece of stick in the time-honoured fashion. Before injecting the bichloride an attempt should be made to aspirate through the hypodermic needle some of the contents of her uterus, so as to give room for the solution to be subsequently injected. She may sometimes be killed by

injections of the bichloride solution into the neighbourhood of her track.

When, as is sometimes the case, her folds lie superficially and can be made out through the skin, it shortens matters very much to cut down on her and draw the loops out carefully, never using much traction, but, if necessary, making two or more incisions to facilitate removal.

Or, if we elect to leave her alone—perhaps because we would like to study the process of parturition I have described, or to examine and experiment with her embryos—it is well to encourage the emptying of the uterus by frequent water-douching. When the young are no longer emitted in response to this stimulus, it will be found that she herself will no longer resist energetically attempts at extraction. You can wind her out then with less risk of rupture or subsequent inflammation.

On the whole you will find that the familiar obstetric aphorism, "meddlesome midwifery is bad," applies to the parturient Guinea-worm just as appropriately as it does to the parturient woman.

The next illustration I shall select of a parasite, or disease germ, which, after being voided into water, enters an intermediary and subsequently a human host, is afforded by the lung fluke—*Paragonimus westermanni*. I select this parasite because it has, or may have, a special interest for Americans.

My first acquaintance with this trematode was in 1880. I was then in practice in Amoy, China. At that particular time I was interested in the subject of hæmoptysis, and availed myself of every opportunity

to examine with the microscope blood coughed up from the lungs in phthisis, in heart disease, or in any other morbid condition that turned up either in hospital or in private practice.

On one occasion I was consulted by a Chinaman, a petty mandarin, about an eruption between his fingers, to wit, the itch. While I was engaged in examining his hands my patient began to cough. He hawked up, and, after the manner of his race, incontinentally expectorated the result of his efforts on to my study carpet. I observed that the expectorated material was red and viscid; and so, instead of reproaching him for spitting on my carpet, requested him to repeat the cough and this time to deposit the sputum in a watch-glass. He very obligingly did so. My forbearance was rewarded. On placing a little of the rusty sputum under the microscope I found it to be loaded with little brown, operculated bodies, manifestly the ova of a parasite.

On interrogating my Chinese friend he told me he was a native of Foochow, but had of late years resided in North Formosa. He had come to Amoy quite recently. The blood-spitting, he told me, began in Formosa. He told me further that he knew of a number of similar cases there. Evidently the disease had been acquired in Formosa, and was probably endemic there. He said that every morning on waking he coughed up an ounce or more of the viscid brown material, and during the day smaller quantities of the same description of sputum. He told me that more than once since the cough began he had brought up suddenly large quantities of bright red blood, and that this was not an unusual feature of the disease as he had seen it in Formosa.

About this time I had in hospital a Portuguese who suffered from some obscure thoracic trouble. I suspected aneurism. The patient had, like my blood-spitting Chinese friend, come from North Formosa. He got a certain amount of relief from rest and iodide, and desiring to return to his home, in Tamsui, I gave him a letter to my friend Dr. Ringer, who was in practice there at the time. I mentioned my tentative diagnosis, and requested him to clear it up by a post-mortem examination if such could be obtained. The man died, and Dr. Ringer made the autopsy. In his account of this Dr. Ringer told me, among other things, that in making a section of the lungs he had come across a minute, fleshy, slightly flattened oval body, grey in colour, and about a quarter of an inch in length, which at the time appeared to be alive, for, as he watched it, he saw some brownish material expelled from a minute orifice near one end of the flattened surface. Suspecting the nature of this body, I asked Dr. Ringer to send it to me if he had not thrown it away. In due course I received the specimen preserved in spirit, and had the satisfaction of finding in the sediment of the spirit, brown, oval, operculated ova identical in all respects with those which my Chinese patient had so obligingly provided some time before. I sent the parasite to Dr. Cobbold, the leading English helminthologist of that day, who, believing it was new to science, very appropriately named it *Distomum ringeri*.

When I stumbled across this Formosan disease I was not aware that a short time before my observations were made Professor Baelz, of Tokio, had encountered the same disease in Japan. He had not seen the parental form, and, supposing the ova in the sputa were some

form of gregarine, had named the disease *Gregarinosis pulmonum*. On submitting specimens of the ova to Leuckart, that distinguished naturalist recognised their true nature. Later on, parental forms turning up in Japan, it was found that the supposed new distome had been seen many years before and described under the name *Paragonimus westermanni*, the first specimens having been procured from the lungs of a tiger.

Paragonimus westermanni.

Gradually information has been accumulating about this disease, and we now know that it occurs not only in North Formosa and Japan, but in Korea, also possibly in China, and, moreover, that it has appeared in the United States of America. As regards the United States, so far there is no record of its occurrence in man, but, according to Ward and others, it has been found in cats, dogs, and pigs. Possibly it may have occurred in man; or, possibly, the disease being of recent introduction into the States, man as yet has not been infected. That he will by-and-bye be infected there can be little doubt. Therefore I would advise you to bear this parasite in mind should

you come across a case of chronic non-tubercular blood spitting, and to examine the sputum with the microscope on the chance that it may contain the ova of *Paragonimus westermanni*.

On making a post-mortem examination of these parasitic blood spitters, what are known as the burrows of the parasite are found in the lungs, principally towards the periphery of the organs. There may be only one such burrow or there may be many, in the latter case the lungs being seriously damaged. The so-called burrows are little tumours or, rather, thickenings produced by inflammatory exudate in the parenchyma of the lung. They may be as large or even larger than a walnut. The tumours are riddled with the small passages or burrows in which the parasites lie. These passages communicate with the bronchi into which the ova-laden muco-sanguineous material bathing the parasites escapes.

Ova of *Paragonimus westermann*.

According to the degree of the infection is the gravity of the disease. It may be inconvenient only; or it may be very grave from the recurring attacks of profuse hæmoptysis to which the patients are liable; or it may predispose to some other form of pulmonary disease. It goes on for years. Rarely are the parasites themselves coughed up, although every day a certain amount of the rusty, ova-bearing sputum is expectorated or swallowed.

Apart from the lung condition *Paragonimus westermanni* is responsible for other and even more serious

mischief. The lung is evidently its normal habitat; but this parasite, like so many others, is a wanderer in its youth, and may lose its way in the human body. Thus it sometimes strays into important organs which are manifestly unsuitable for its biologic requirements. In these organs it forms characteristic burrows in the irritated, infiltrated tissues. Thus it has been found in such localities as the scrotum, the liver, and also in the brain. Should it stray into the last-mentioned organ, it will necessarily give rise to grave nervous disease—such as Jacksonian epilepsy and other signs of intracraneal tumour, and will ultimately cause death.

Unfortunately the life history of this important parasite, beyond the first and final stages, has not been ascertained. We know that the first step is made in water. I had no difficulty in procuring abundant supplies of the sputum from my Chinese patient for experimental purposes. Reflecting on what might be the natural destiny of sputum cast on the ground, I concluded that it must be in one of three directions. First, it may dry up and, so far as the ova it may contain are concerned, perish. Second, it may be eaten by some animal. Third, it may be washed down by rain or otherwise, and so get into wells or pools of water. I experimented in the direction suggested by the last consideration. I found that if the sputum is mixed with water and the water changed occasionally, after some weeks, more or fewer according to temperature, a ciliated embryo developed in each egg. By-and-bye the embryo emerged from the egg by forcing back the operculum closing in one end of the shell. It then swam about with great energy for many hours. Beyond this, not being in the endemic region, I could not follow its career; but analogy

indicates that, if fortunate, the ciliated embryo gets into some fresh-water animal, possibly a small mollusc, in which it undergoes the well-known evolutionary changes characteristic of the distomes. When these are completed it finds its way in water, or encysted perhaps on some water plant, back to man again.

It is important from the standpoint of prevention that the life history of *Paragonimus westermanni* be worked out, for, once lodged in the human body, our power over it is at an end. In the event of Jacksonian epilepsy or other evidence of intracraneal tumour appearing in a subject of endemic hæmoptysis there is ground for assuming that the symptoms are produced by the invasion of the brain by this parasite. In such a case, and if there are localising symptoms, there is distinct justification for an attempt to remove the verminous tumour by surgical measures.

III.

Bilharziosis: Filariasis.

The same consideration that led me to bring forward *Paragonimus westermanni* and the endemic hæmoptysis with which it is associated, induces me to give yet another illustration of the conveyance of a disease germ through water, and probably by a fresh-water intermediary.

We now know that Bilharzia disease, similar to if not identical with that which is so common in Africa, occurs in America; many cases have been reported in the West India Islands, particularly in Porto Rico. Quite recently another and possibly widely diffused, but specifically different, species of the same genus has been added to the already sufficiently long list of human disease germs. The new species, which gives rise to very different and grave lesions, has been named *Schistosomum cattoi*, and also *Schistosomum japonicum*. It is possible that it, too, may occur in, or if it does not already occur in, that it may in the near future be introduced into the Western Hemisphere.

As yet it is impossible to estimate the importance of the new parasite, but there can be no question as to the importance of the more familiar species of Bilharzia, at least as regards Africa, where in places, Egypt for example, it affects one half of the population.

The introduction into America of Bilharzia, or, as it is more correctly called, *Schistosomum hæmatobium*, may

have been a recent occurrence; hence its non-recognition long ago and its present limited geographical range in this part of the world. If this be so, a serious situation has arisen, for, as with many other disease germs of old world origin, Bilharzia may yet spread far and wide over your Continent, and in congenial spots prove as serious an enemy to health in America as it undoubtedly is in Africa and its dependencies.

Schistosomum hæmatobium—Male.
(*From a photo by Dr. T. S. Kerr.*)

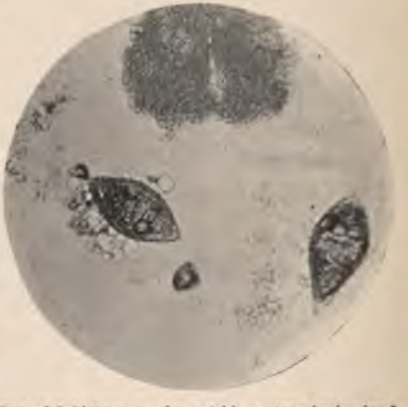
Schistosomum hæmatobium is a trematode or fluke. Unlike most trematodes, which are hermaphrodite, it is bisexual, the female worm, a comparatively long and slender organism, living partly and more or less permanently embraced by the infolded lateral borders of the shorter and stouter male. The female is about 20 mm. in length and the male about 15 mm. Thus the head and tail of the female come to project, so to speak, beyond the head and tail of the male.

Schistosomum hæmatobium—Female.
(*From a photo by Dr. T. S. Kerr.*)

Schistosomum hæmatobium—Male and Female. (*After Loos.*)

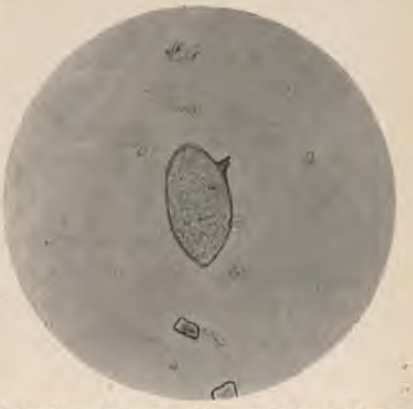
The principal habitat of the parasite is believed to be the portal vein, its radicles and their anastomotic connections about the region of the bladder and rectum. In any given case there may be only a few, or there may be many parasites present, and there is, generally speaking, a corresponding degree of gravity in the morbid effects produced. These effects are brought about by the parasites in their endeavours to place their eggs in the medium—fresh water—suitable for hatching purposes; in other words, in their efforts to secure the continuation of their species by passing from one human host to another human host.

There is no certainty about the exact details of the process of oviposition; much is conjecture. It would appear that after attaining the portal vessels by some as yet unknown route, the mature parasites move up against the blood stream until they get to the hæmorrhoidal or vesical venous radicles and their connections. Arrived at the smallest



Ova of *Schistosomum hæmatobium*—terminal spined.

vessels into which the coupled worms can enter, the female contrives somehow to get her eggs through the walls of the smaller veins and into the perivascular connective tissue, whence the eggs, aided possibly by the spine with which they are furnished, work their way towards the mucous surfaces, and so into the urine or fæces, as the case may be. The process is attended with inflammatory trouble and a good deal of oozing of blood, and urinary or rectal irritation is produced. The ova thus set free escape from the body of the human host in the excretions.



Lateral-spined ovum—*Schistosomum hæmatobium.* (*From a photo by Dr. T. S. Kerr.*)

If you get a patient affected with the vesical form of Bilharzia disease to pass water into a urine glass, on holding the glass up to the light you will perceive little mucoid shreds, or even little clots of blood, floating in the urine. These mucoid shreds and the muco-sanguineous deposit in the glass under a low power of the microscope will show the ova in abundance. Perhaps the best plan for arriving rapidly at a diagnosis, or to obtain specimens for experiment, is to get the patient to nearly empty his bladder and then to catch in a watchglass the last few drops he can expel with straining. These last few drops are generally tinged with blood, and are almost sure to contain many ova.

On placing one of these ova under the microscope, you can easily make out that it contains a ciliated embryo or myracidium, as it is called. You can see it move from time to time. Now, although you get this indication of life, so long as it remains in the urine there may be no further indication of progress in development; but if you dilute the urine with a little fresh water at once a change commences. The little embryo becomes excited, squirming about very actively, and, rupturing the shell of the egg, finally escapes into the surrounding fluid. In this it promptly proceeds to rush and gyrate about as if in search of something. Manifestly this is the first step *Schistosomum hæmatobium* makes in its extracorporeal life; the first step towards another human host. The step is made in fresh water.

This much is positively known, and very important knowledge it is; but the rest of the life history of this dangerous and troublesome parasite is a blank. Many investigators have tried to fill it in. Analogy and reason suggest that from the water the embryo passes into some fresh-water animal. That this is the case is extremely probable, but so far this animal has not been recognised. If it be an animal, it is evidently one with peculiar geographical limitations. Even in the endemic area it is only within circumscribed districts that the disease can be acquired. In these circumstances we have a kind of clue to the identification of the hypothetical intermediary. It is to be hoped that ere long this clue will be successfully followed up. On the success of the quest depends intelligent, economical, and effective prophylaxis.

It has long been known that whereas the Bilharzia eggs that escape in the urine have their spines placed

terminally, those that escape in the fæces have their spines placed laterally. I cannot affirm that this arrangement of the spine in the vesical and rectal ova respectively invariably obtains, but it certainly does so in a large number of instances. Speaking for myself, I have never seen a lateral-spined ovum in the urine, but I have often seen them in the fæces. In some instances in which the rectum alone was affected, and in which there were no ova in the urine, all the ova were lateral-spined.

Schistosomum cattoi—Male.
(From a photo by Mr. E. E. Henderson.)

It has been suggested that this difference in the position of the spine in vesical and rectal bilharziosis respectively is brought about by the different mechanical conditions in which the parental worms ovulate, by the influence of pressure in altering the position of the ovum in respect to the duct of the shell gland. This may be the explanation. I doubt it. It may be that in this difference in the position of the spine in vesical and rectal bilharziosis we have an indication of difference of species; that there is a species of Bilharzia specially affecting the bladder and producing terminal-spined ova, and another species that specially affects the rectum and produces lateral-spined ova only. I have only once seen

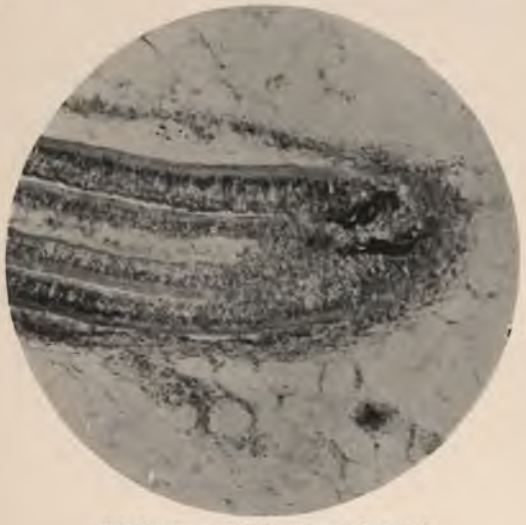
a case of Bilharzia disease acquired in the Western Hemisphere—in the West Indies. In this case the rectum alone was affected. Although the patient was kept under close observation for several weeks, and his urine was frequently examined, the urine never showed any ova, but the fæces invariably yielded characteristically lateral-spined eggs. I confess it is difficult to understand how

Schistosomum cattoi in mesenteric vessel.
(*From a photo by Mr. E. E. Henderson.*)

or why the same species should produce lateral-spined ova when it haunts the rectum, and terminal-spined ova when it haunts the bladder. I am tempted to conjecture that we may be dealing with two or more distinct species, and that the American Bilharzia belongs to the lateral-spined species.*

* This conjecture is encouraged by the recent investigations of Dr. Gunn, who has met with many examples of rectal bilharziosis in Porto Ricans. In every instance the ova were lateral-spined, and in no instance were ova found in the urine.

A further argument in favour of there being a multiplicity of species of Bilharzia infecting human beings has cropped up quite recently in the discovery, to which I have already referred, of *Schistosomum cattoi*. Eastern Asia was long believed to be free from Bilharzia disease, and so it is as regards *Schistosomum hæmatobium*, and also as regards the hypothetical lateral-spined ovum pro-

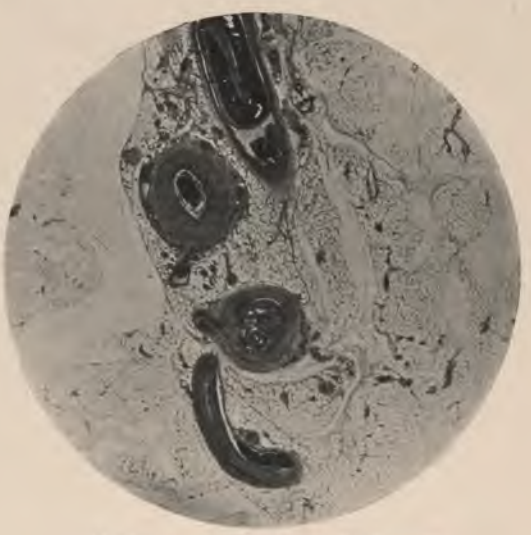


Schistosomum cattoi in mesenteric vessel.
(*From a photo by Mr. E. E. Henderson.*)

ducing species; but we now know that Asia has a species of Bilharzia of its own, namely, this *Schistosomum cattoi*.

The new parasite, like the more familiar Bilharzia, inhabits the blood vessels connected with the portal system; but whereas hæmatobium lies on the venous side of the capillaries, cattoi lies for the most part, if not altogether, on the arterial side. In appearance and habit both species closely resemble each other. *S. cattoi* is

somewhat smaller than *S. hæmatobium*, and the male is further distinguished by his smooth non-tuberculated integument. The egg of *S. cattoi* has no spine, being regularly oval and perfectly smooth, and having a much thinner shell. These smooth, non-spined ova the female worm contrives to place in the mucosa and submucosa of the large and small intestine, but especially in the former,

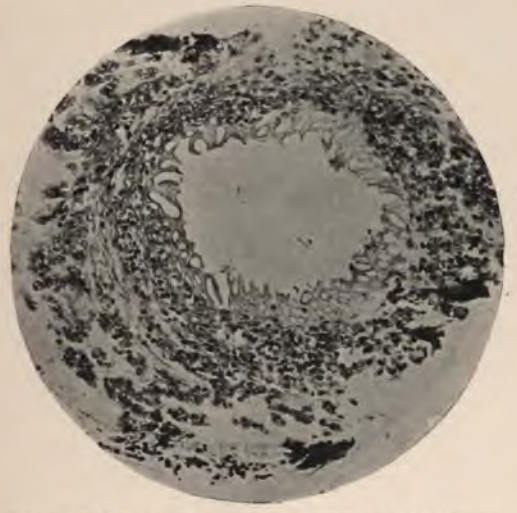


Schistosomum cattoi in vessels of mesentery.
(From a photo by Mr. E. E. Henderson.)

and in such profusion that in places they literally form what looks on section like an almost complete layer in the bowel. So numerous are they that in some microscopical sections of affected tissue, as in those of the appendix vermiformis, they seem to replace completely the normal structures. From this situation the eggs are extruded into the bowel, much in the same way as those of *S. hæmatobium* are extruded into the lumen of the

bladder or bowel. By this route they probably find their way into water, where, it is to be presumed, the ciliated embryo which they contain is liberated and finds its special intermediary, and so back into man or beast.

There can be little doubt that this parasite will prove a serious element in tropical and sub-tropical pathology. It occurs in China and Japan. This has been definitely



Transverse section of appendix vermiformis showing ova of *Schistosomum cattoi.*
(From a photo by Dr. T. S. Kerr.)

ascertained. Probably it occurs elsewhere, as, for example, in the warmer parts of America. In Japan it has been linked up with a peculiar kind of chronic enteritis and anæmia, and is associated with enlargement of the spleen and liver and a fatal cachexia. A diagnosis is arrived at by the discovery of the characteristic ova in the stools of such patients, or post-mortem by microscopical examination of scrapings from the surfaces of the diseased bowel.

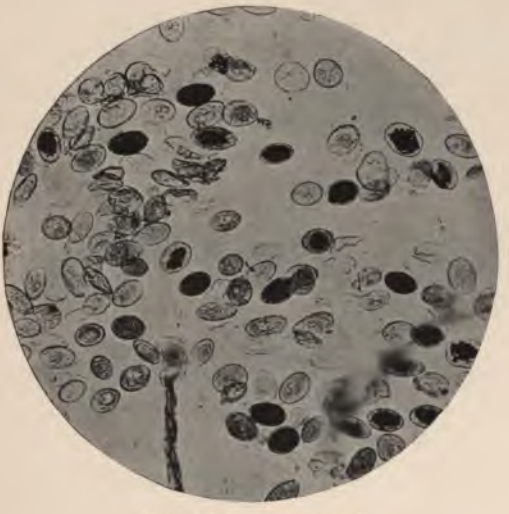
We have information from Japan that cats are liable to this parasite as well as man, just as in the case of *Paragonimus westermanni*. This is a most important fact for Americans, for it is probable that what holds good for *Paragonimus westermanni* holds good for *Schistosomum cattoi*, and that America may be, if she is not so already, invaded by *Schistosomum cattoi*, and that the infection may spread through the agency of the domestic animals as well as by that of man himself.

In speaking of *Paragonimus westermanni*, I suggested that you should be alive to the presence of this parasite in America, and that in cases of non-tubercular hæmoptysis you should examine the sputum with the microscope, on the chance of getting an explanation of the symptoms by the discovery of the presence of the ova of that parasite. I would suggest similarly a microscopical examination of the urine in hæmaturia, and of the fæces in chronic dysenteric-like affections, on the chance of obtaining an explanation of the symptoms by the discovery of the ova of one or other of the Bilharzial parasites alluded to.

Some of the facts I have mentioned in connection with these trematodes bring home to us our helplessness as physicians when such a worm has succeeded in effecting a lodgment in the human body. Others of these facts indicate the necessity for a more complete knowledge of the life histories of the parasites, more especially of their life histories outside the human body during their passage from human host to human host—that is to say, while they are still amenable to our interference. With full knowledge of this we undoubtedly could prevent the diseases to which these parasites give rise. Once acquired we are helpless. We cannot angle for flukes in the portal vein; to kill them *in situ*, even supposing we could,

might lead to dangerous consequences. In such circumstances the most we can hope to effect is to keep the unhappy victim from being injured and from unwittingly injuring himself.

We must bear in mind that such diseases do occur; accustom ourselves to be on the outlook for them; to suspect their presence. We must learn to diagnose them,



Ova of *Schistosomum cattoi.*
(Enlarged from a photo by Mr. E. E. Henderson.)

to confirm or negative such suspicions. And when we do arrive at a positive diagnosis, we must instruct our patient as to the best way to guard himself from injurious methods of treatment and injurious ways of living, and from being a source of danger to his neighbours.

The subject of Bilharzia disease should live quietly, eschew alcohol altogether, eat little or no red meat, salted or otherwise preserved foods of an indigestible nature or

such as are calculated to increase urinary or intestinal irritation. He must guard against chill, against gonorrhœa, and against all causes of cystitis and enteritis. Above all, in the case of bladder bilharziosis he must, so long as possible, keep out of the way of the surgeon who, at all events in a good many instances, is only too keen to get an excuse for passing instruments into the bladder. Only when purulent cystitis is present are we justified in using instruments in this disease. They are only too often the medium of bacterial invasion of the urinary tract, an invasion which otherwise might have been avoided. I have seen much harm from injudicious instrumentation in Bilharzia disease.

During the Boer war many of our English soldiers contracted Bilharzia in South Africa. It is endemic in Natal and in parts of the Transvaal. One poor fellow I saw who, having escaped the Boer bullets, developed symptoms of bilharziosis on the return voyage to England. On landing, and in ignorance of the nature of his complaint, he consulted a surgeon about the urinary irritation and slight hæmaturia he was suffering from. There was no microscopic examination of the urine. The pain and the blood suggested stone. A sound was introduced. No stone was discovered, but a cystitis was communicated and, of course, increased the suffering. Another surgeon was now consulted. He unfortunately discovered some condyloma-like excrescences around the anus. Now Bilharzia produces not only papilomata inside the anus, but at times outside the anus as well, and even on the perineum and groins. The surgeon was not aware of this; but ignoring the urinary trouble, and in spite of the protest of the soldier that such a thing was impossible, he diagnosed syphilis and prescribed calomel. The outcome

of the combined treatments was cystitis and severe salivation and syphilophobia. In examining the urine microscopically there was no difficulty in recognising the Bilharzia ova, and on excising a piece of condylomatous growth the parasitic nature of these was made equally apparent. A little knowledge and a little caution and trouble would have spared the poor man much suffering and some expense.

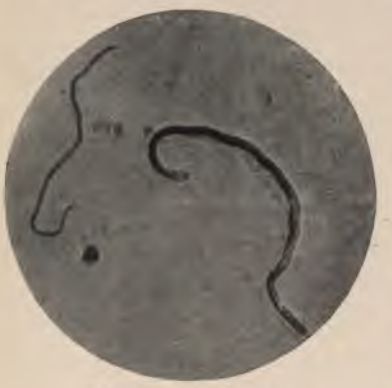
Filaria nocturna.

I pass now to the consideration of another set of tropical disease germs—those whose peculiar geographical range and endemicity is determined by the tropical requirements of special species of insects which remove them from the body, nurse them, and finally re-implant them in a fresh human host.

Filaria diurna.
(From a photo by Dr. T. S. Kerr.)

Even more complicated than those I have already alluded to are the processes by which the blood worms and the parasites of malaria pass from man to man. In their case the intermediary—the mosquito—serves not only as foster-mother and medium for developmental change, but also as abstracting and re-implanting agent.

The blood of tropical man is liable to be infested by the embryos of at least four distinct species of nematode worms. These embryos are named respectively *Filaria nocturna*, *Filaria diurna*, *Filaria perstans*, and *Filaria demarquai*. They have many features in common; nevertheless experts can readily distinguish them one from the other.



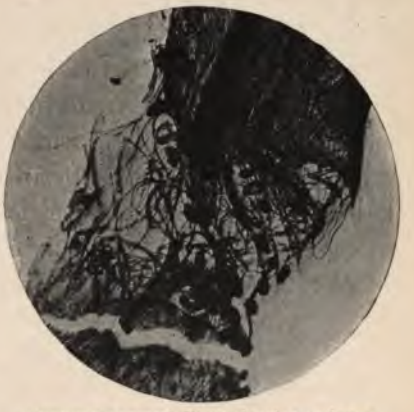
Filaria diurna and *perstans*.

F. nocturna is found pretty well all over the tropics and sub-tropics; *F. diurna* is peculiar to West Africa; *F. perstans* is also an African species but occurs in Demerara; *F. demarquai* is an American species, being confined, so far as we know, to certain of the West India Islands and to Demerara; possibly it occurs in New Guinea and other tropical countries.

Of these several blood worms *F. nocturna* is the best known. As it is infinitely the most important, as well as the most common, I shall confine my remarks on the blood worms to it. Doubtless the life histories of the other three species, though still very imperfectly known, resemble that of *F. nocturna*.

Filaria demarquai.

If you examine microscopically the blood of the dogs in certain countries, more especially of South China, in a large proportion of them you will find, sometimes in prodigious numbers, hundreds in every drop, minute, colourless, almost structureless, eel-like, wriggling organisms, measuring about one-hundredth of an inch in length and rather less than the three-thousandth part of an inch in breadth. If you kill one of these dogs and open its heart you will find in the right auricle and ventricle, and perhaps extending far into the pulmonary artery, two or more, or even a great bundle of inter-twined worms. Unravel this verminous bundle. You will find that the worms appear to be of two kinds—a larger, measuring about a foot in length by about a twelfth of an inch in breadth, and a smaller, measuring about eight inches in length by about a sixteenth of an inch in breadth. You will also find that all the smaller kind are provided with peculiar corkscrew-like tails. The smaller corkscrew-tailed worms are the males; the larger straight-tailed worms are the females. The name of this worm is *Filaria immitis*. If you select one of the larger or female worms and examine her carefully with the microscope, you will find that her uterus is crammed with young at various stages of development, those near the vagina resembling in every



Ruptured parental filaria showing embryos.
(From a Photo by Dr. T. S. Kerr.)

particular the little wriggling organisms you had previously found free in the blood stream. You conclude that the free wriggling organisms in the blood are the progeny of the parental worms lying in the right side of the heart. The relationship is easily established.

If you find similar embryo worms, say *F. nocturna*, in the blood of a man, analogy justifies the inference that these, too, are the progeny of larger parental worms living and breeding somewhere in the tissues or in some structure more or less intimately connected with the circulation. As a matter of fact we know that the parental form of *F. nocturna* lives in the lymphatic trunks of the body and limbs. They have been found there a good many times, and sometimes in considerable numbers, the males and females being generally in close association, perhaps twined about each other, forming a tiny bundle like so many loosely ravelled strings or hairs. They are long—three to four inches—and about as thick as a horse hair. They have received the name *Filaria bancrofti*. They pour their young—*F. nocturna*—into the lymphatic stream, along which they are carried into the thoracic duct, and so into the blood.

The free embryos never do any harm; but the parental forms, by obstructing and otherwise damaging the lymphatic trunks, often do a very great deal of damage, giving rise to that large group of tropical diseases known as the elephantoid diseases, and almost certainly to that scourge of many parts of the tropics—endemic elephantiasis. In view of the mischief they work it becomes a matter, not only of scientific interest, but of practical moment, to ascertain the way in which the parasite, that is to say the germ of these diseases, is acquired and spread.

Elephantiasis of Scalp.

From photos by Dr. Allardice McDonald, Zanzibar.)

Occasionally the embryo filaria—that is to say *Filaria nocturna*—is found in the urine. But this is a comparatively rare occurrence, and only in the somewhat rare disease known as Chyluria; and even if the parasite does find its way occasionally into the urine, when found there it is always in a languid and moribund state, and evidently in an uncongenial element. Occasionally it is found in chylous or lymphous discharges from the skin. But these conditions are so exceptional, so rare, that, considering the frequency of the parasite in many places, it is in the highest degree improbable that nature should rely on the off-chance of such an opportunity to set the young worm on its way to maturity in another human host. How then does this germ pass from man to man?

Filarial varicose groin gland.

In the endemic areas ten per cent. is not an uncommon proportion of the population to be found affected with filariasis. Thirty per cent.

Elephantiasis of scrotum.

Elephantiasis of Mamma—right leg and foot also affected.
(*From a photo by Dr. Davies, Samoa.*)

Elephantiasis of legs and scrotum, and right arm slightly affected.
(*From a photo by Dr. Turner, Samoa.*)

Elephantiasis of the scrotum, left leg slightly affected.
(*From a photo by Dr. Turner, Samoa.*)

Elephantiasis of upper extremity.

and even fifty per cent. may be affected. In many of the Pacific Islands—the Samoa group for example—I believe even this proportion is exceeded. This being so, the distributing agency must be correspondingly common.

It is evident that the embryo cannot escape into the outer world spontaneously, or by any effort of its own; for, if you regard it attentively under a high power of the microscope, you will find that it is enclosed in a long loose sac in which it can move backwards and forwards, but which it is powerless to quit. It is effectually muzzled by this sac, and thereby absolutely prevented from piercing and so escaping from the vessels.

Seeing then that the embryo worm is not extruded from the human host like Bilharzia, that it cannot escape spontaneously like the Guinea-worm embryo, and that to continue its species it must pass from its human host, we are forced to conclude that some extraneous agency comes to its assistance. What may that agency be?

A study of the habits of the parasite, of the location of its embryos in the human body, and of its geographical distribution, will help us in our search for this agency.

Select a man in whose blood you have found the young filaria. Sample his blood from hour to hour, counting the little worms in a measured quantity of the blood. Keep a register of the number of filariæ you find in each sample of blood. Keep on doing this for a week, a month, a year, taking care meanwhile that the man is in good health, and that he observes normal habits as regards the hours of sleeping and waking. You will very soon satisfy yourself that the filaria exhibits a very definite periodicity as regards its presence in the peripheral circulation.

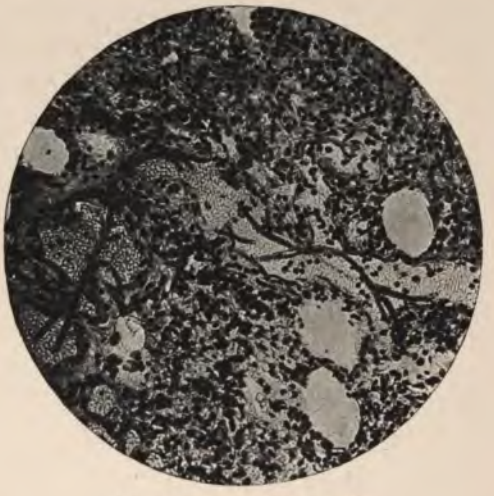
You will find that it is present in enormous numbers—perhaps three or four hundred per drop—at midnight; that

it is practically absent at midday; that it begins to put in an appearance about six or seven in the evening, gradually increasing in numbers up to about midnight, and gradually decreasing in numbers up to about seven or eight in the morning; and that it is almost entirely absent from eight or nine a.m till about six or seven p.m.

The question is often asked, what becomes of the embryo filaria during its temporary absence from the peripheral circulation during the day? Is its disappearance attributable to its death, or does it retire for the time being to the internal organs? The question was answered some years ago.

A coloured man came to London seeking relief from two enormous sub-fluctuating tumours produced by dilated lymphatics connected with the glands of both groins. The tumours were so large and so liable to inflammation that he was practically debarred from earning his living as a sailor. This condition of the groin glands is one of the many troubles caused by the filaria. The blood of the patient on examination was found to contain vast numbers of the young parasites. Repeated observation definitely determined that these embryos came into the peripheral circulation about six in the evening and left it about eight in the morning. One morning, about eight o'clock—that is to say, just at the time the filariæ were accustomed to retire for the day—the poor fellow committed suicide by swallowing a bottleful of hydrocyanic acid. Death was instantaneous. The post-mortem examination was made very soon after. No embryo filariæ could be found in the blood from the peripheral vessels, none in the blood from the liver or spleen, very few in the kidneys and brain; but in the blood expressed from the lungs, in sections of the lungs, in the aortic blood, in

blood from the heart and in the vessels of the heart muscle, but especially in the lungs, they were found in thousands in every drop. The worms therefore retire during the day to the lungs and larger blood vessels. How it is that they are able to maintain their position there I cannot presume to say, but certain it is that by some unknown method they do stem the blood current.



Filaria nocturna in lung vessels.

There is yet another question that is often asked in this connection, namely, what is it that brings about this singular periodicity? Why should the worms leave their day haunt and seek the peripheral circulation during the night?

As regards the first question no satisfactory explanation has so far been forthcoming. Some have suggested that during sleep the peripheral vessels are dilated, and so permit the entrance of the worms. In favour of this

hypothesis has been adduced the fact, and it is a fact, that if a filarial patient is made to sleep during the day and wake during the night, the periodicity of his parasites is correspondingly inverted; they then come into the peripheral blood during the day and disappear from it during the night. But then how explain the fact that in ordinary circumstances, as regards sleeping and waking, the parasites begin to come into the peripheral blood about six p.m., that is some three or four hours before the usual bed-time, and begin to disappear from the circulation soon after midnight, that is when sleep is soundest and many hours before the usual time of waking? And, again, how explain another fact, namely, the periodicity of *F. diurna* which is exactly the opposite of that of *F. nocturna?* These two specifically distinct embryo filariæ resemble each other so closely in size, structure, and movement, that it is practically impossible to distinguish them with a microscope, and yet one is a day worm and the other is a night worm. If the vessels are too small to admit *F. nocturna* during the day, how comes it that they freely admit *F. diurna?* Another curious difficulty in getting at the explanation of filarial periodicity has cropped up lately. In the case of *F. nocturna,* as I have mentioned, by changing the hours of sleeping and waking the periodicity is easily and quickly inverted; but a similar change of the habits of the host has no corresponding effect in inverting the periodicity of *F. diurna.* You may get the subject of diurna infection to sleep during the day and keep awake during the night; but, in spite of this, the parasites continue to disappear from the blood during the night and reappear during the day, just as if the patient were observing ordinary habits.

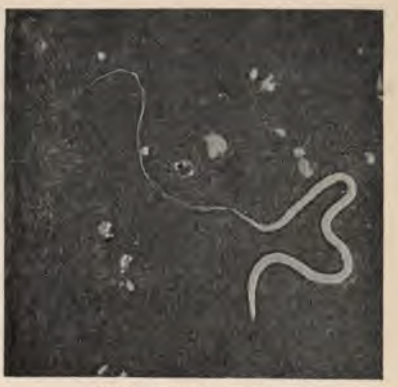
Although we cannot indicate the cause—mechanical, chemical, or vital—of filarial periodicity, we may be assured that it is an arrangement in the interest of the parasite.

I have said that the filaria is not spontaneously extruded from the body, that it cannot itself effect its escape from the body, but that somehow it must get out of the body; and I inferred from this that some extraneous

Head of Culex.

agency must interfere to remove it. Seeing that the habitat of the filaria is the blood, we infer that this extraneous agency must be something that naturally abstracts the blood. And seeing that the filariæ come to the surface of the body—the only situation accessible—during the night only, we are driven to the inference that the abstracting agency must be a blood-eater or blood-sucker of nocturnal habits, and that it operates through the skin. Further, this blood-sucker of nocturnal habits must

have a geographical range corresponding to that of the filaria—that is to say, be indigenous to the tropics and sub-tropics.



Filaria leaving sheath.

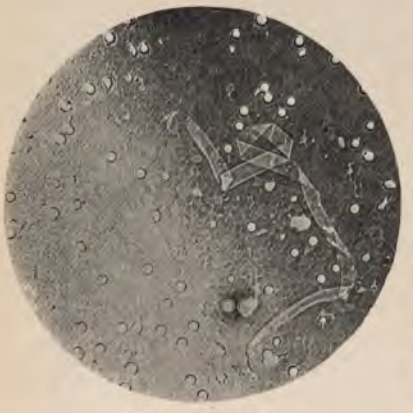
Reasoning in this way we are driven to the conclusion that the external agency that abstracts the filaria is the mosquito—or rather one or more tropical or sub-tropical species of mosquito.

This conclusion can be readily tested by a very simple, but very interesting and instructive experiment.

Filaria has left its sheath.

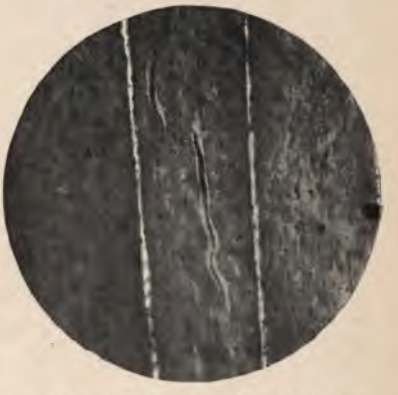
Secure the co-operation of some complacent individual in whose blood you have already ascertained that *F. nocturna* abounds. Put him to bed under an efficient mosquito net, and let loose on him about eleven or twelve o'clock at night a swarm of the common tropical mosquito (*Culex fatigans*), which you have previously reared from the egg and which had not previously fed on blood. By next morning the mosquitoes will have fed, and are now gorged with blood and are clinging to the mosquito netting. Catch them care-

fully in wide-mouthed bottles; place a little water and a piece of fresh banana in each bottle for food and drink and egg-laying purposes. Change the banana every day or two. Keep the bottles in a dark place and in a temperature of about 80° Fahr. Remove one or more mosquitoes daily for dissection or section. With a little practice you will be able to make beautiful microscopical preparations from which you can read the story of the life of the filaria in the mosquito as in a book; you will be able to trace its evolution from the moment it enters the insect to the stage at which it is ready to leave it and be re-implanted by the mosquito into another human host.



The empty sheath.

The first step in this evolutionary process is perhaps the most interesting, showing, as it does, the marvellous adaptiveness of nature, the ingenuity, if I may use such an expression, she exercises in overcoming difficulties and in attaining her end.



Filaria in thoracic muscles of Mosquito.

I have already pointed out that the young filaria while in the human host is enclosed in a loosely fitting sac in which it can move backwards and forwards with great freedom. The sac is much longer than the worm it encloses. On close scrutiny with high powers of the microscope you will be able to make out that the blunt or head end of the worm is provided with a short and delicate spine and also with a circlet of hooked lips. You can see that both spine and hooklets, or rather lips, are protractile and retractile. The sheath in which the filaria is enclosed is, I believe, a provision designed to prevent the premature use of this armament on the blood vessels of the human host and the consequent escape of the worm into the tissues, where it would be beyond the reach of the friendly mosquito. On entering the mosquito's midgut, or, as it is generally called, stomach, the first thing the filaria does is to get rid of this muzzling sheath, and so uncover its formidable head armature

Filaria in thoracic muscles of Mosquito.

Filaria in thoracic muscles of Mosquito.

Soon after it has been drawn up through the proboscis, in consequence of the absorption of a considerable part of the water it contains and the diffusion of the hæmoglobin under the action of the digestive juices, the blood in the stomach of the mosquito becomes thickened and acquires a viscid consistency. The filariæ at once perceive the change in the mechanical condition of the medium in

Filaria in thoracic muscles of Mosquito.

which they are swimming. They become violently excited, and rush backwards and forwards in their enclosing sacs, which are now held, so to speak, by the viscidity of the blood. The little animals are evidently making frantic efforts to get out of their sheaths. Retiring to the tail end of their sheaths ever and anon they rush forward, butting the head end with great violence. The sheath is no longer carried before the head as it was when in the fluid blood of the human blood vessels. It is held by the thickened blood. The attempts

Filaria in thoracic muscles of Mosquito.
(From a photo by Mr. H. Spitta.)

to escape are renewed again and again with increasing vigour, till at last the head end of the sheath gives way and the little worm swims free in the viscid mass. At

Filaria in thorax.

once it steers a straight course for the wall of the mosquito's stomach. This it attacks with spine and hooks, and, quickly piercing it, bores its way through. Within a few hours it has found its way to the thoracic muscles, in which it comes to rest between the fibres. Here it lies for a fortnight or longer undergoing great developmental evolution. In the course of ten days to a fortnight or three weeks it acquires an alimentary canal and greatly increases in size. When these changes have been effected

Filaria in prothorax of Mosquito.

the now formidable-looking worm resumes its travels, working its way to the head of the mosquito and finally passing down into the labium or sheath of the proboscis. In this situation it lies outstretched patiently waiting for an opportunity to escape. This opportunity comes when the mosquito next proceeds to feed on man. Into the little puncture in the skin which the mosquito makes the filaria passes by breaking through the delicate membrane that unites the two labellæ that form the distal end of the labium, and so once more it returns to a human host. Ultimately it finds its way to the lymphatic trunks where

Filaria in proboscis of Mosquito.

the sexes come together and the young are born. These in their turn find their way into the circulation, and there await their chance of a visit from the mosquito.

Filaria in proboscis of Mosquito.

In this way the filaria passes from man to man, and in this way the elephantoid diseases are acquired and communicated.

The knowledge is a sure and certain guide to efficient prophylaxis.

Not less wonderful and practically significant is the story of the malaria parasite, which I shall attempt to narrate in my next lecture.

Embryo filaria as it leaves Mosquito.

IV.

Malaria.

The story of the filaria is both interesting and important. Even more important, and quite as interesting, is the story of the malaria parasite, which, indeed, that of the filaria foreshadowed. Both parasites are in their immature stages prisoners in the blood. Both are incapable of leaving the human body spontaneously, and both are incapable of re-entering the human body by any effort of their own. Both are equally dependent on the friendly offices of the mosquito to transfer them from host to host, and to nurse and develop them during the passage.

Thus, although in a zoological sense widely different, the filaria and the malaria parasite, as regards their biological requirements, are at one period of their respective lives closely akin; and in the case of both parasites these requirements are satisfied by the same insect agency and very much in the same way.

If you examine systematically with the microscope the blood of a patient who has not been taking quinine recently and who is suffering from malarial fever—let us say benign tertian, and commence your examinations an hour or thereby before the onset of the anticipated rigor, and if you exercise a little patience and skill, and have a good oil immersion lens at your disposal, you should have no difficulty in seeing the parasite. Much depends on the way you prepare your blood-slides. Slip and cover-glass should be perfectly clean, and the finger you prick should

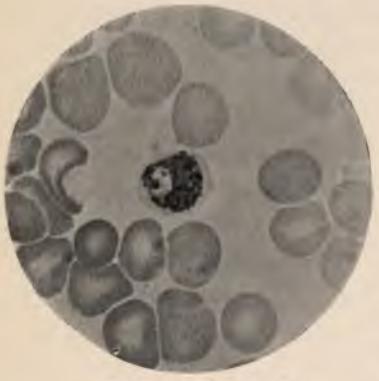
also be clean. The droplet of blood you work with should be no bigger than a fair-sized pin's head. You should touch the droplet —not the skin—lightly with the centre of the cover-glass, which should then be placed gently on to the slip. The blood will now run out between the glasses in an exceedingly delicate film in which the corpuscles are disposed in a single layer and lying flat, and therefore in the most favourable position for the observer to perceive anything abnormal in their interiors. When it is seen that the blood has spread itself out sufficiently it is well to ring the cover-glass with vaseline so as to prevent evaporation, movement of the corpuscles, and their too great compression.

Ring Parasite

In slides so prepared, although you may have to search field after field, you are sure sooner or later to come across the malaria parasite. Perhaps you will notice that some of the red cells are rather larger and lighter in colour than the others. Scrutinise one of these big pale cells carefully. You will probably make out that the greater part of the corpuscle is occupied by a large and still paler body, and that this body is dotted over with minute grains or very short rods of black or very dark red pigment. This is the mature form of the tertian

Benign Tertian Parasite half grown

malaria parasite. There may be very few of these bodies in the slide—one in every twenty or thirty fields—or they may be so numerous that one or two examples are to be found in every field of the microscope.



Benign Tertian Parasite, Three parts grown.

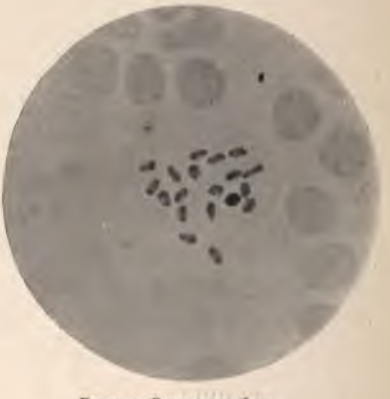
Procure another slide of the same patient's blood about an hour later, say during the earlier stage of the rigor. You will again come across in your examination bodies similar to the foregoing, but in the later preparation you will perceive that pigment and pale substance have undergone changes in their respective arrangements. The pigment grains are now concentrated into one or two clumps, and the pale substance constituting the mass of the parasite has arranged itself into a cluster of some twelve to twenty little spherules. This is what is known as the rosette body. The spherules are the spores of the parasite; the pigment is excrementitious matter. Following up in successive blood films, prepared from hour to hour, the evolution of the little body, you will find that about the time of rigor the rosette body breaks up, the constituent spores, or, rather, those of them that escape the phagocytes, attaching themselves to other and hitherto uninfected red corpuscles. These corpuscles the spores contrive to enter and at once commence to grow at the

Rosette.

expense of the hæmoglobin. In the early stages especially they show active amœboid movement. Presently grains of dark pigment appear in the interior of the growing parasites. As the parasites increase in size amœboid activity slows down, pigment becomes more abundant, and by the end of the second day the parasite has acquired the appearance and size of the body encountered when the series of examinations was commenced. This is the cycle of the benign tertian malaria parasite in the blood. In the absence of treatment it may be renewed again and again and for many generations.

Rosettes.

We can understand how in this way the malaria parasite, once it has succeeded in obtaining a footing, reproduces and maintains itself in the human body. So far, however, there is nothing in the structure or behaviour of the parasite that might guide us in conjecturing as to how it passes from one human host to another as, of necessity, it must do if it is to maintain itself in existence as a species.

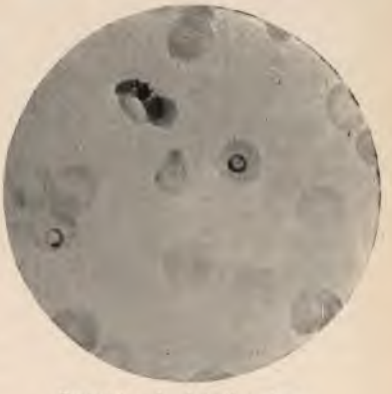


Rosette, Spores set free.

To aid us in understanding how this neces-

sary passage from host to host is effected I would ask you to select for the supply of the necessary material a case of what is known as malignant or sub-tertian malaria. It is true that in benign tertian and quartan malaria the little drama which I shall attempt to describe is also enacted; but in these it is not so easily and conveniently followed as it is in the malignant infection. The case selected should be one of some standing; fever should have been present during at least a week or ten days.

From such a case prepare blood films in the way already described. On examining these you will probably encounter certain pale crescent-shaped bodies, each crescent carrying about its centre a cluster of black pigment grains. On careful examination you will be able to make out that the crescent has rounded-off horns, and that it is enclosed in a red blood corpuscle. The enclosing corpuscle may be difficult to recognise, owing to the circumstance that it has lost much of its hæmoglobin and is misshapen. As the crescent is longer than the diameter of a normal red blood corpuscle, it follows that the corpuscle that includes the crescent is stretched and proportionately deformed. The convexity of the crescent is closely applied on one side to the rim of the corpuscle, and the circular outline of the corpuscle on this side is fairly preserved; but on the other side, the side of the concavity of the crescent,



Crescent and sub-tertian rings.

the contour of the including corpuscle is somewhat fattened as it stretches across from horn to horn of the crescent. The point to be more particularly noted is that the parasite is enclosed in a blood corpuscle.

After a little experience you will probably remark that there are two kinds of crescents, one slim and elegant in shape, in which the pigment is arranged in a little circle or, it may be, compact clump; another, a shorter and squatter kind, in which the pigment is coarser and less concentrated.

When you have learned to recognise these two types of crescent, procure two microscopes. In the field of one microscope place one of the longer and more elegant type of crescent, that in which the pigment is concentrated; in the field of the other microscope place one of the squat crescents in which the pigment is coarse and scattered. Make your preparations rapidly, so as to be in good time to observe the ensuing changes, which, be it remembered, sometimes are effected somewhat rapidly. Do not move the slides, but pass from one microscope to the other observing the ensuing changes.

In successful preparations, in the majority of cases and in both instances, the crescents will be seen gradually to become squatter and more kidney-shaped. Then they become oval, and finally spherical, the enclosing blood corpuscle rupturing or otherwise disappearing. In the crescent with concentrated pigment, which has a somewhat granular appearance, the pigment remains concentrated, often arranged as a ring at the centre of the sphere. It undergoes no further change unless it be—an unfortunate and by no means uncommon occurrence—that it is taken up by some prowling phagocyte by which it is broken up and destroyed.

In the sphere derived from the crescent with scattered pigment, and which apart from the pigment has a hyaline appearance, the pigment becomes still more diffused. Later on in this type of crescent-derived sphere the individual grains of pigment begin to exhibit movement which, from moment to moment, increases in activity. At last the movement seems to be communicated to the body of the sphere itself, which now begins to be jerked about and to writhe, as it were, under the influence of some unseen internal force. It looks as if it were intensely excited. Suddenly from its periphery a number of long waving filaments are projected. These whip-like filaments are at first attached to the sphere by one end. They knock about the neighbouring red corpuscles by their waving, lashing, jerking movements. Presently one or more of the filaments, or flagella, as they are sometimes called, break away and swim about freely in the blood plasma. By degrees the movements of any flagella that may not have succeeded in breaking away slow down; very likely, just as in the case of the other type of sphere, the phagocytes, for which these flagellated bodies appear to possess a great attraction, come and engulf it.

Flagellating Body.

This evolution of sphere and flagellated body from the crescent parasite is a very remarkable phenomenon. But perhaps the most remarkable fact about it is that it

takes place only after the blood has been removed from the blood vessels. The spherical bodies and the flagellated bodies are never observed in blood immediately on its removal from the circulation; nor is the crescent body, while still a crescent body, ever observed to be attacked and included by the phagocyte in the peripheral circulation.

A manifest inference from this is that the process of sphere and flagellum formation which we can witness on our microscope slides belongs, under natural conditions, to the life of the malarial parasite outside the human body; and that the location of the sphere in the interior of a red blood corpuscle is a provision for preserving it from the attacks of the phagocytes while inside the human body.

Flagellating Body and free Flagellum.

Let us return for a moment to the embryo filaria I spoke about in my last lecture. I pointed out to you then that the filaria while in the human body is enclosed in a loose sac or sheath, very much in the same way as the crescent malaria parasite is enclosed in a red blood corpuscle. In both instances it is evident that the arrangement is one in the interests of the parasite. Without its sac the filaria would escape from the blood vessels into the tissues, where it would be beyond the reach of the mosquito; without its covering blood corpuscle the malaria parasite would be devoured by the phagocytes. Without its special protection the filaria would commit suicide;

without its special protection the malaria parasite would be murdered. The end would be the same in both cases, namely, destruction.

By a little management we can get the filaria to cast its sheath while on our microscope slides, just as we can get the malarial crescent to cast its enclosing corpuscle in similar circumstances. The experiment is a very striking one. I would strongly recommend those of you who may have the opportunity to repeat it.

Select a filarial case in which the stock of filariæ is large. Late in the evening, that is to say when the parasites abound in the peripheral blood, prepare in the usual way a number of rather thick blood slides. Ring the cover glasses with vaseline or oil, and wrap each slide separately in thick blotting paper in such a way that the blotting paper does not smear the oil or vaseline. Place the slides in a small tin box and lay the box on a block of ice in a cool room in which the temperature of the air is between 32° and 40° Fahr. The slides must not be frozen, only chilled. Leave the slides on the ice all night. Next morning examine them under the microscope, using, say, a half-inch objective. If the chilling has been successfully conducted, you will find that in most of the slides, in places or uniformly, the blood has become lakey and therefore viscid; that is to say, the hæmoglobin has escaped from the stroma of the blood corpuscles and is diffused in the liquor sanguinis, thereby thickening it. The chilled filariæ are lying passive or only moving slowly in the cold, lakey blood. By degrees, as the temperature of the slides rises in the warm atmosphere of the laboratory, the filariæ will become more active, finally very active, and will then commence the butting movement I described when speaking of the conduct of

the parasite in the thickened blood in the mosquito's stomach. One after the other in the course of the day they will break through the head end of their sheaths, and swim about in the blood plasma in the same way as the free flagella of the malaria parasite do.

Now up to this point the situation, the conditions, the requirements, and the behaviour of the filaria and of the malaria parasite are practically identical. So similar are they that it seems reasonable to suppose that perhaps beyond this point the parallelism may be still further maintained. Let us try then, experimentally, if the mosquito will subserve the malaria parasite as it subserves the filaria. To give the experiment the best chance of success we will conform to the known habits of malaria, and select for our experiment a species of mosquito having a geographical range and distribution corresponding to those of malaria, one belonging to the family Anophelina—say, *Anopheles maculipennis*. We set a number of these anophelines to bite a patient in whose blood the crescent parasite is present. We are careful to keep the insects under appropriate conditions and to feed them from time to time on blood or on fruit. We dissect them at serial intervals, and we

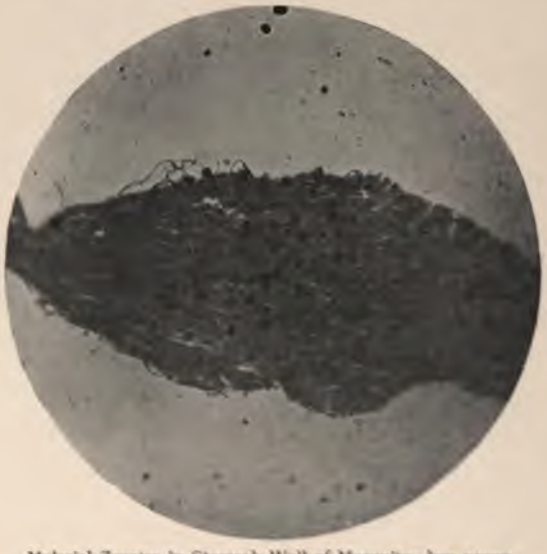
Anopheles Mosquito.

try with the microscope to follow the destiny of the crescents which the insects must have swallowed in the blood they had imbibed. In other words, we repeat in human malaria Ross's classical experiment in bird malaria.

At short intervals of a few minutes, or, later, of a few hours, we tear out the midgut or stomach of a series of the gorged insects and express on to slides the contained blood. Therein, just as in the blood taken directly from the finger tip of the patient, we can follow the transformation of the crescents into spheres, and a proportion of the spheres into flagellated bodies. We can see the flagella break away from their parent spheres and wriggle about through the blood. And now, if we are lucky, we may witness a new and very striking phenomenon rarely seen in finger blood. We may see the free flagella deliberately seek out and crowd around the non-flagellating spheres which they proceed in an excited manner to butt energetically as if seeking an entrance. We may see one of the spheres protrude a minute papilla, as if to solicit and receive the impact of one of the butting flagella. Presently into this papilla a flagellum slips. It wriggles about for a time and then, after disturbing temporarily the contents of the sphere, comes to rest and disappears from view. Meanwhile the papilla is withdrawn, and although the other flagella for a time continue their attentions to the sphere, entrance is denied them. For this important observation we are indebted to a distinguished American pathologist—Mac Callum.

Manifestly this is a sexual phenomenon; it is an act of impregnation. The malaria parasite is therefore bi-sexual. The flagellated sphere is the male; the non-flagellated sphere is the female; the flagella are spermatozoids; and the mosquito's stomach is the copulating ground.

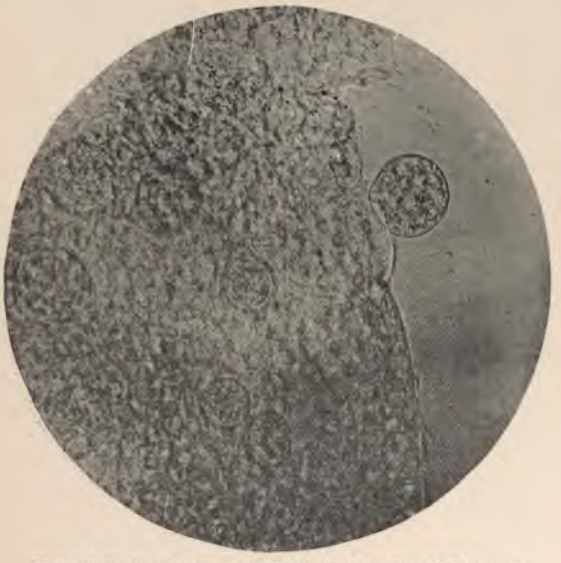
Continuing your observations on the impregnated sphere, you will find that gradually the pigment it contains moves to one pole of the sphere which now begins to assume an oval shape. Then one end of the oval, that opposite to the end at which the pigment has accumulated, becomes pointed. The little body becomes elongated and shaped like a spear-head. Concurrently with this change in form it begins to move, slowly at first,



Malarial Zygotes in Stomach Wall of Mosquito—low power.

more rapidly later; and if we could follow its career we would see, as may be inferred from sections and preparations of the mosquito's stomach, that it attacks the epithelial coating of this organ, passes through this coat, finally bringing up in the outer or muscular layer. Arrived here it settles down, assumes an oval and then a spherical form and acquires a capsule. Day by day it grows until at the end of ten or twelve days it has acquired compara-

tively large dimensions, so large indeed that the muscular coat of the insect's stomach can no longer accommodate it. As a consequence of this enormous increase in size, the sphere comes to protrude on the outer surface of the stomach, like a wart, or like a big wen on a bald scalp. At the early stage of its encystment a one-twelfth immersion lens was required to detect the parasite, but at

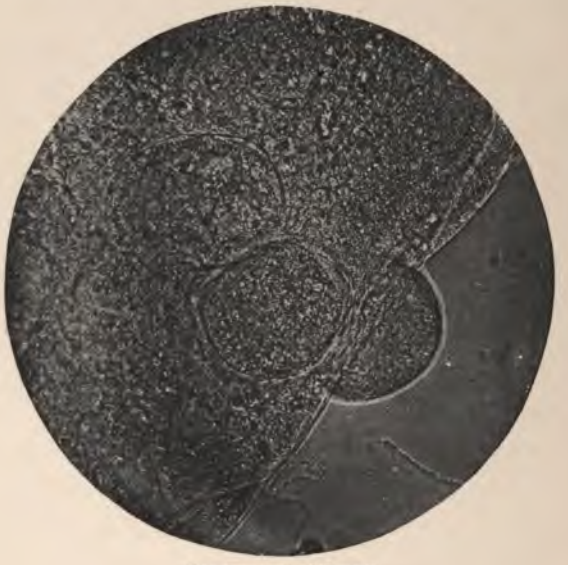


Malarial Zygotes in Stomach Wall of Mosquito—high power.

this later stage the cyst has become so large that it can be readily seen with an inch objective.

In a heavily infected stomach dozens of such cysts can be recognised protruding from the outer surface. Concurrently with the relatively enormous increase in the size of the parasite certain changes are effected in its interior. By repeated multiple division the contents become converted into a large number of minute spherules,

each of which, when the process of subdivision is completed, becomes covered with a pile of thickly-set minute elongated spindle-shaped rods arranged like the spines on a hedgehog or sea-urchin. Finally the spherules disappear; so that when the parasite has attained its full size it consists merely of a capsule packed with innumerable minute rods. The capsule is now tense. It ruptures. The



Development of Zygote.

swarm of rods it contained is discharged into the body cavity of the mosquito, whence, by way of the blood, they are carried to certain glands—the salivary glands—situated in the fore part of the thorax of the insect. The cells of these glands remove the rods from the blood. The rods may be seen in great numbers lying in the big, plump salivary cells. Thence they get into the secretion of the glands—the saliva—where they may also be detected.

What next? The position of these little rods, or sporozoites, justifies us in presuming that when the mosquito proceeds to make a meal on a human victim the sporozoites pass with the saliva along the salivary ducts, down the proboscis, and so into the blood stream of the bitten individual.

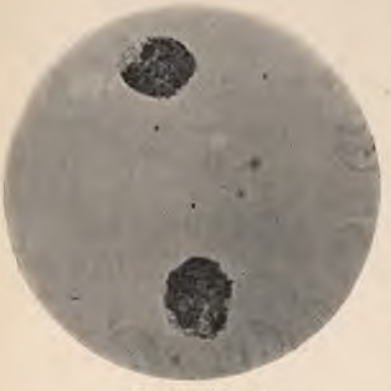
Let us try by experiment if this conjecture can be substantiated. Set one of your mosquitoes, some ten or

Oocyst containing Sporozoites.

twelve days after it has fed on the crescent-containing blood, to bite a man who has never had malarial fever, and await the result. From a week to a fortnight later the bitten man will get typical malarial fever, and you will find the parasites characteristic of malaria in his blood.

If you would still further satisfy yourself about the

nature and destiny of the sporozoites, repeat one of Schaudinn's beautiful experiments. Go out rowing till you blister your hands. Return to your mosquitoes. Select one that had its malarial meal ten or twelve days previously. Dissect out on a glass slide its salivary glands, teasing the latter up in a drop of serum obtained from your blistered hand. Add a trace of blood from your finger to the serum. Apply a cover glass; ring the preparation with vaseline; place it on the warm stage, and watch. Some of the little rods set free in the serum will attack the blood corpuscles, enter them, and, changing form, assume the amœboid form of the human phase of the malaria parasite.



Gametes—Tertian.

Such is the life cycle of the malaria parasite, the latter part of it so curiously resembling that of the young filaria. Every step of it has been followed over and over again with the microscope, and the final step, the infection of man by infected mosquitoes, has been proved by direct experiment conducted with the most rigid precautions against possible sources of fallacy. It has been proved up to the hilt.

The malaria parasite then has a double cycle, one passed in man for the multiplication of the parasite and its maintenance in the human host; one passed in the mosquito, also for multiplication, but principally for the passage of the parasite from human host to human host.

The human phase, sometimes called the endogenous phase, is asexual; the mosquito phase, sometimes called the exogenous phase, is sexual.

Naturalists recognise in this complicated double-life cycle of the malaria parasite a close resemblance to the double-life cycle of the Coccidiidæ. Accordingly they have applied to its various phases and elements a corresponding nomenclature. Thus the term *Schizogony* is given to the human cycle as a whole, the individual organism being called a *Schizont*, and the spores into which it breaks up at maturity *Merozoites*. The sexual elements of the mosquito cycle are called *Gametocytes* —abbreviated *Gametes*, the male being termed *Microgametocyte*, the female *Macrogametocyte*. The flagella which the microgametocyte projects are called *Microgametes*, and the single cell of which the macrogametocyte is composed a *Macrogamete*. The fertilised macrogamete is called a *Zygote*, and the zygote when it has acquired powers of locomotion is called an *Ookinet*. The ookinet encysted in the mosquito's stomach wall is an *Oocyst*, within which are developed the *Sporoblasts* or spherules which ultimately evolve the *Sporozoites*.

Although the malaria parasite resembles the coccidia in many particulars, it has been found convenient to classify it along with a number of similar blood parasites of the lower animals into a distinct

sub-order, sometimes called *Hæmosporidia*, sometimes *Hæmocytozoa*.

These are terms somewhat hard to remember, but as they are constantly employed nowadays in our extensive and rapidly-growing malaria literature, the student, if he would understand what he reads, must make himself familiar with them and their exact application.

Time will not permit me to enter into the cytology or other biological points in connection with this important disease germ whose life history I have attempted to describe, but before passing to my next subject I would say a few words on certain points bearing on the practical application of the facts alluded to.

The malaria parasite is transmitted by a special kind of mosquito; not by every kind of mosquito. To avoid malaria we must therefore, among other things, avoid this special kind of mosquito. The first step towards this is to learn to recognise these mosquitoes and to acquaint ourselves with their habits.

There are some three or four hundred described species of mosquito, and probably half as many undescribed species. Fortunately, only a small proportion of these are effective malaria intermediaries. All of these malaria intermediaries belong to one easily recognised sub-family—*Anophelina*. Of the anophelines there are eighty known species. Only a limited number of these eighty species are malaria carriers—that is to say, so far as we know; it is well, however, to regard all anophelines with suspicion.

If you examine the head of a mosquito with a pocket lens you will make out without much difficulty that it has five mouth appendages. These are a central—the proboscis; two outer—one on each side of the pro-

boscis—the antennæ; and two between the antennæ and the proboscis—the palps. The male mosquito, which does not suck blood and is therefore not directly concerned in the transmission of malaria, is readily recognised by his bushy, plumose antennæ; in the female — the blood-sucker — the antennæ are almost naked. The palps are the organs by which the Anophelinæ are most readily and surely recognised. In the female anophelines the palps are about as long as the proboscis. This is an easily recognised and absolutely distinguishing feature. In all other mosquitoes the palps in the female, and in some genera in the male also, are either rudimentary or very much shorter than the proboscis. By attention to this point you can at once tell a malaria-transmitting from a non-malaria-transmitting species of mosquito.

All mosquitoes have certain habits in common, anophelines among the rest. Their individual activity and the activity of the developmental processes are readily affected by temperature, being favoured by moderate warmth, and retarded or altogether arrested by cold. This remark applies equally to any malaria parasites the mosquito may chance to harbour.

In favourable conditions the eggs laid on still water by the mosquito hatch in from two to four days. The resulting larvæ being very voracious grow rapidly and, after casting their skins several times, enter, in about ten days' time, on the pupa stage; from this after two days more they emerge full-grown insects.

The larva of the anophelines is, like the insect, easily recognised. When at rest it lies parallel with the surface of the water, whereas the larvæ of most other mosquitoes hang, so to speak, by their tails from the surface.

Let us imagine a primitive native community—a village in some district in which anopheles mosquitoes abound; for example, a negro village on the West Coast of Africa. Let us suppose that by some happy and very improbable chance this village is free from malaria. A stranger with malarial gametes in his blood comes to the village. The local anopheles bite him and become infected and infective. In a very short time every soul in that village gets malaria. There is much sickness, and there are deaths not a few. After some years, and after many re-inoculations by infected mosquitoes, the surviving original inhabitants gradually acquire immunity from malaria and the parasite can no longer be found in their blood. Meanwhile children are born in the village. They have no immunity, and therefore, soon after birth, being bitten by the infected anopheles, acquire the infection. In the course of years they too become immune. Meanwhile other children are born, are bitten, and become infected. In this way there is kept up in the village a permanent stock of infected anopheles. This is the condition of every village in every highly malarious district; the adults are immune, the children are nearly all of them full of malaria parasites, and a large proportion of the village mosquitoes are infective.

The practical lesson to be drawn from this is that in a malarious district the neighbourhood of a native village should be shunned, especially during the evening, night, and early morning, when anopheles are most active.

The adult native of a highly malarious district, so far as malaria is concerned, is generally a safe companion; he has no parasites in his blood, having acquired immunity by repeated inoculations in youth. But the adult

native of a less highly malarious district is not always a safe companion, for in him the process of immunisation may not be complete, and he may possibly be the subject of an existing infection. Anyone, black man or white man, who has malaria parasites in his blood may become a centre of infection, and is therefore a danger to his neighbours wherever anopheles are about. He should therefore be protected from mosquito bite and actively treated.

Imagine an island in mid-ocean, far away from any malarial continent. It has its own special insect pests, mosquitoes among them, but there are no anopheles. Malaria therefore is unknown. On an evil day for the island a fast-steaming ship arrives and introduces—perhaps as larvæ in a water-tank, or in a neglected water-bottle in some unoccupied passenger cabin, or otherwise—the cursed insect. The hydraulic and climatic conditions are favourable and the anopheles multiply apace. Presently in some coolie labourer from India or China, or in some native returned from service in a foreign country, or in sailor, or traveller, malarial gametes come on the scene. The anopheles, now numerous, become infected, the inhabitants get malaria, and the island, formerly noted for its salubrity, becomes a by-word for unhealthiness.

This is no fancy picture. For centuries after its discovery and colonisation Mauritius was noted for its beauty, its delightful climate, and for its salubrity. There were no anopheles there in the days of Paul and Virginia. Situated in the middle of the Indian Ocean, far away from continental influences, it enjoyed an equable climate well suited to recruit the broken-down anæmic constitution of the victim of tropical disease. So high

was its reputation for salubrity that up to the early sixties, in times when Europe was not so accessible as it is at the present day, it was used as a sanatorium by the British in India. Of course many of the invalid soldiers and civilians who visited the island, and many of the imported Indians who laboured on the extensive sugar plantations for which Mauritius was famous, must have introduced, times without number, malaria parasites. In those happier days, there being no anopheles present, any imported parasites did not spread; they died out. But about the time I mention, that is to say in the early sixties, anopheles were introduced; how, is not known. Gradually they spread over the island, carrying the malaria germ with them. A big epidemic was the consequence, and now malaria is endemic in Mauritius, and large areas of this former sanatorium are extremely unhealthy.

With the increasing opportunities of these modern days for rapid travel and communication, many islands and isolated districts at present healthy will at no distant date share the fate of Mauritius unless, before it is too late, effective measures are taken to prevent the introduction of anopheles.

In view of her extensive and growing relations with the islands of the Pacific, America has a special interest in this matter. Let British experience in Mauritius be a warning to you.

In tropical countries in which there is no cold season or very hot dry season—dry heat is just as inimical as cold is to the mosquito—infective insects may be found all the year round; consequently, in such places, malaria is perennial. But in sub-tropical or temperate climates in which there is a cold winter there can be no continuity

in the propagation of malaria by the mosquito. There must therefore be some way by which in these countries the parasite bridges over what, to it, is the inimical period of the year. This is effected in one, possibly in two ways.

The malaria parasite once introduced into man may persist, and usually does persist, for many months, sometimes for one or even two years, possibly longer. After this it dies out unless re-infection by mosquito intermediary takes place. During the time the parasite continues to live in the human body it is sometimes quiescent and disappears from the peripheral circulation; sometimes it is active and reappears in the peripheral circulation. Unless interfered with by treatment, each time it comes into the peripheral circulation it produces gametes—that is, sexual forms—and consequently at that time can infect the mosquito. Thus an infection contracted last year may be communicated during a relapse to the mosquito of this year; and so the winter is bridged.

It has been suggested that there may be yet other ways by which the difficulty of the mosquito-dormant season may be got over. Some authorities maintain that a proportion of the sporozoites, set free when the oocyst ruptures into the body cavity of the mosquito, find their way into the ova of the insect and so into the larva and adult. A similar thing happens, we know, in the case of the pyrosoma of Texas Fever and other tick-conveyed pyrosoma infections. Although this conjecture has not been confirmed it is worth following up, for it is not wanting in probability and in support from analogy. If it be well founded, and if the malaria parasite can support the cold of winter as well as the mosquito or mosquito larva do, then when the mosquito, evolved from an infected

larva, enters on active habits in the following spring, the malaria parasites it contains may reach a human host.

The question is often asked, Is there any other way by which malaria can be contracted than through mosquito bite? For many reasons, I believe not. It is difficult to prove a negative; but, so far, there is no observation capable of bearing investigation that would lead us to suppose that malaria can be acquired, under natural conditions, except by mosquito bite.

It is also sometimes asked, Do the lower animals suffer from malaria? That they are subject to infections by similar hæmocytozoa is well known, but it is not known that any of them suffer from parasites specifically identical with those of human malaria. It is possible that the anthropoid apes, or some mammal that has been closely associated with man from the beginning of their mutual evolution from their common ancestor, will yet be found to do so.

The great practical value of the facts I have mentioned is patent to every thoughtful man. A clear conception of the life-history of the malaria parasite, ability to recognise the special kind of mosquito that conveys the parasite, common sense, a little money, and we should be able in virtue of this knowledge to abolish malaria in any co-operating community.

V.

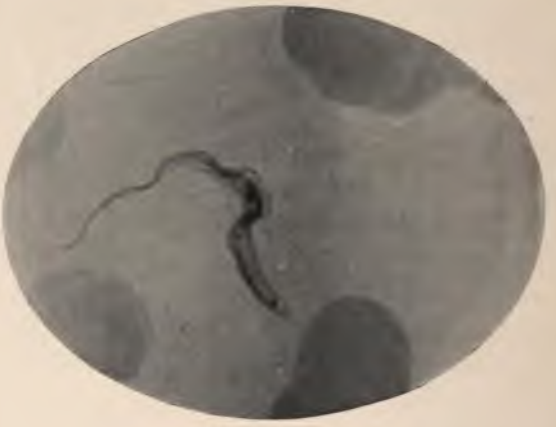
Trypanosomiasis and Sleeping Sickness.

Some years ago it might have been said, having regard especially to the organisms alluded to in the foregoing lectures, that our knowledge of tropical disease germs—particularly the most important of these, that of malaria, of their physical characters, of the way they leave the human body and the way they re-enter the human body, was fairly complete. Here and there, no doubt, there were important gaps; but the leading facts, especially those having a practical bearing—that is, having a bearing on treatment and prophylaxis—had been definitely settled. A sort of completeness seemed to have been attained. But within the last three or four years any hope of finality that formerly might have been cherished has been rudely upset, and, instead of being able to lie back and fold our hands with some measure of satisfaction in completed work, we have once more to take to our laboratories and to our microscopes.

Two new diseases (new, of course, only in the sense of being newly discovered) classifiable as tropical have lately been sprung upon us. I allude to trypanosomiasis and to tropical febrile splenomegaly or, as it is now generally called, Kala-Azar, and their associated conditions. Besides these absolutely new diseases,

important and revolutionary knowledge has been acquired in connection with an old and long-known disease, especially important to America; I allude to Yellow Fever. In this and my next lecture I propose to deal with Trypanosomiasis and Kala-Azar more particularly from the standpoint of etiology.

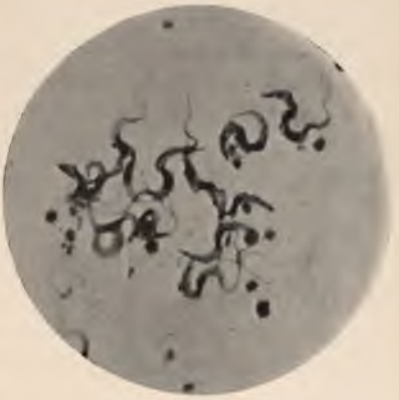
In May, 1901, Dr. Forde, a Colonial Surgeon in the River Gambia Colony in West Africa, was puzzled about the case of an Englishman who suffered from



Trypanosome.

an irregular chronic fever, supposed to be malarial. Quinine had failed. To help to clear up diagnosis Dr. Forde examined the patient's blood with the microscope, and therein came across a very minute wriggling organism the nature of which he failed to recognise. The patient returned to England. After six months' furlough he again went back to the Gambia, still suffering from time to time from relapses of his old fever. Still puzzled about the case and especially

about the organisms found in the blood, which he concluded had something to do with the symptoms, Dr. Forde called to his assistance the late Dr. Dutton, then engaged on malarial work in the colony. Dr. Dutton at once recognised the nature of the little wriggling bodies and also the importance of the discovery. Although a French observer, Nepveu, had probably seen the same or a similar parasite in man some ten years previously, this was the first occasion on which it was definitely recognised that man was liable to infection by trypanosomes—for such was the nature of the parasite Dr. Forde had found in his patient's blood.



Trypanosomes.
(*From a Photo by Dr. T. S. Kerr.*)

I have no intention of giving a detailed description of this class of parasite; such can be found in books on Natural History. Suffice it to say that the trypanosomes are minute protozoal organisms shaped like an elongated spindle, with a long lash or flagellum at one end and a delicate fin-like swimming membrane running from the attachment of the flagellum to the other end of the spindle. For the most part they are about the length, exclusive of the flagellum, of the diameter of a blood corpuscle. They swim very actively in the blood plasma with a wriggling screw-like movement, the flagellum being usually in front.

Little is known of their life history further than that they multiply in the blood by longitudinal division, and that some of them are conveyed from vertebrate host to vertebrate host by biting insects. We know little of their sexual reproduction; the little we do know is in great measure conjectural. Some of them are pathogenic; others, as for example that of the rat —*T. lewisi*, are not.

To return to the patient. He was sent home to England, where Dr. Dutton made a careful study of the parasite and of the associated clinical phenomena. Dr. Dutton named the parasite *Trypanosoma gambiense* and the disease Trypanosomiasis.

I had an opportunity of seeing this case in Liverpool in August, 1902. The clinical tableau was so striking that one could not but wonder how it was that its special nature had not been appreciated and its special cause suspected, if not recognised, long ago.

The patient told a story of long standing, chronic irregular fever with occasional intervals of complete apyrexia. The temperature chart during the febrile periods showed the usual evening rise to 100° Fahr. or 101° Fahr., occasionally higher, and the morning drop to normal or sub-normal. The pulse was rapid and feeble, and there was complaint of intense muscular weakness, of palpitations, and of breathlessness. On stripping the patient for examination, what struck me most were the great patches of ill-defined erythema irregularly distributed over limbs and trunk. Some of the patches had a distinctly-ringed appearance, and may have been seven or eight inches in diameter; other patches, some as large as the palm of the hand, were not circinate, being simply uniform blotches of congestion. In neither rings

nor patches were the margins of the erythema abruptly defined; they shaded off gradually into normal skin. Here and there, but particularly in the area of the erythematous patches, there was an ill-defined œdema, best recognised if viewed from a distance. The face was puffy. The spleen was enlarged. The patient lived for some months longer, and ultimately died of pneumonia.

Two months after, through Dr. Dutton's courtesy, I had seen this patient I was consulted in October, 1902, about a case of chronic fever which for long had been supposed to be malarial. The patient, a lady, had lived for some time on the Upper Congo. The story she gave was that up to the autumn of 1901, although she might have had one or two mild attacks of malarial fever which yielded readily to quinine, she had enjoyed fair health. On August 14th of that year she was bitten on the leg by some animal, believed to be a fly. Although at first the part became very painful and swollen, under soothing treatment the local irritation slowly subsided. A fortnight later she had the first of a long series of febrile attacks which came and went, uninfluenced by quinine, until her death two years and three months after the date of the bite to which she attributed her illness. When I first saw her in October, 1902, fourteen months after the onset of the disease, she was, although weak, able to get about a little. Her spleen was very much enlarged, her face was puffy, and scattered over her limbs and trunk I recognised the same type of erythema I had seen in Forde and Dutton's case. Suspecting the nature of the disease, I sent her to hospital, where her symptoms and, more especially, her blood could be closely studied. Many microscopical

examinations of the latter were made, but beyond a marked large mononuclear leucocytosis at first nothing peculiar was discovered. After a week Dr. Daniels encountered a solitary but unmistakable trypanosome, and subsequently, probably in consequence of greater familiarity with the technique, we could nearly always find similar parasites in suitably prepared blood films. Occasionally none could be found; generally two or three were present in every film, occasionally as many as seven or eight.

Some years before this I had seen another case with symptoms exactly similar to the foregoing, namely recurring febrile attacks, erythema multiforme, enlargement of the spleen, weakness. The patient was a lady missionary. She too had resided on the Congo, and she too, prior to the oncoming of her symptoms, had been bitten on the leg by some poisonous insect. She had returned to the Congo. I wrote for information about her and was told that her symptoms continued, and that Dr. Broeden had found the trypanosome in her blood.

Since that time other and similar cases have been met with in Europeans in or from Tropical Africa, so that now it may be definitely concluded that the symptom syndrom of—

1. Chronic irregular fever,
2. Erythema in rings, patches, or rubeoloid spots,
3. Local œdema,
4. Tachycardia,
5. Muscular weakness,
6. Enlargement of the spleen,
7. Anæmia,
8. Enlargement of lymphatic glands,

occurring in a patient from Tropical Africa practically means infection with *Trypanosoma gambiense*.

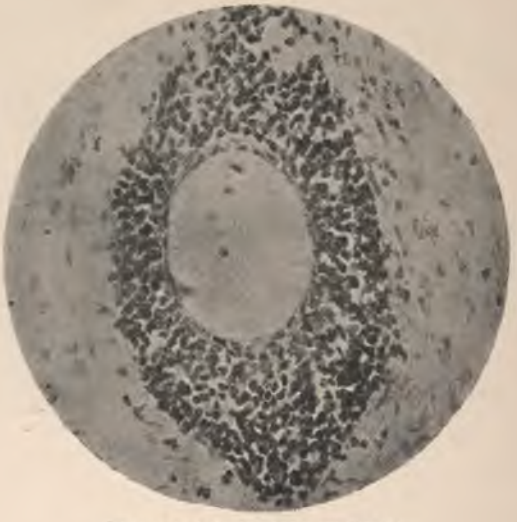
For upwards of a century students of tropical pathology have puzzled over a peculiar and very striking African disease, somewhat inaccurately described by its popular name, the Sleeping Sickness. Its weirdness and dreadful fatality have gained for it a place not in medical literature only, but also in general literature. The mystery of its origin, its slow but sure advance, the prolonged life in death that often characterises its terminal phases, and its inevitable issue, have appealed to the imagination of the novelist, who more than once has brought it on his mimic stage, draping it, perhaps, as the fitting Nemesis of evil doing.

Sleeping Sickness.
(*After Brumpt.*)

The leading features of this strange sickness are such as might be produced by a chronic meningo-encephalitis. Low irregular febrile disturbance, headache, lassitude deepening into profound physical and mental lethargy, muscular tremor, spasm, paresis, sopor, ultimately wasting, bedsores, and death by epileptiform seizure, or by exhaustion, or by some intercurrent infection. In every case the lymphatic glands, especially the cervical, are enlarged, though it may be but slightly. In many cases pruritus is marked. In all lethargy is the dominating feature.

In some respects this disease, which runs its course

in from three months to three years from the oncoming of decided symptoms, resembles the general paralysis of the insane. It differs from this, however, in the absence, as a rule, of the peculiar psychical phenomena of that disease. There are exceptions; but, generally, though the mental faculties in Sleeping Sickness are dull and slow-acting, the patient has no mania, no delusions, no optimism. So far is the last from being the case, that

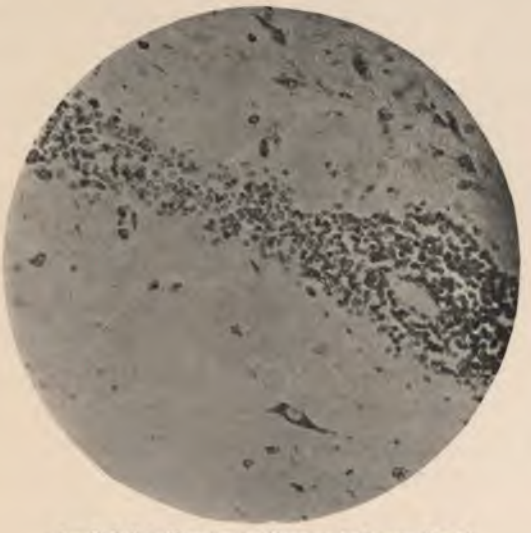


Lesions in Sleeping Sickness (Brain).
(*After Mott.*)

he is painfully aware of his condition and of the miserable fate in store for him; and he looks as if he knew it.

Post-mortem the naked-eye evidences of intracranial disease are not always, or even usually, very marked. Milkiness of the meninges, sometimes a little inflammatory effusion and congestion of the pia mater and arach-

noid may be seen; rarely are any gross inflammatory lesions discovered. But on microscopical examination, as was first pointed out by a distinguished British pathologist, Dr. F. Mott, definite evidence of a universal meningo-encephalitis, in the form of a small cell perivascular infiltration, can readily be recognised. Dr. Mott has further shown that this condition is not confined to the brain and cord, but may be present throughout the



Small Cell Infiltration in Sleeping Sickness (Brain).
(*After Mott.*)

entire body, and in every tissue in which lymphatics occur. This discovery fully explains the symptoms of the disease.

Until recently Sleeping Sickness was confined, so far as we knew and know, to the west of Tropical Africa, from Senegambia to Benguela. It occurred here and there among the negro tribes, for the most part in those

a little back from the coast. In the endemic districts it would from time to time break out epidemically, attacking and almost depopulating the villages; in other instances its occurrence was more sporadic. In the days of the slave trade many poor wretches died of Sleeping Sickness during the voyage across the Atlantic. Nor were the slaves safe after landing in America or in the West Indies. Months, sometimes years afterwards, and after a long spell of apparent good health, Sleeping Sickness would develop in some of the plantation hands and run its usual fatal course. But, and this is a remarkable and significant circumstance, the disease never spread to those negroes who had been born in America or the West Indies and who had never been to Africa. It was absolutely confined to negroes who had come from Africa. Manifestly the negro brought the germ, or cause, with him; manifestly this germ could remain latent in the body for a period of years; and, seeing that the disease was not communicated to his fellow slaves, the America or West India born negroes, it is equally manifest that the transmitting agency, whatever it might be, was either not present or not effective in America.

Not long after the opening up of the interior of the Dark Continent, and apparently in consequence of the resulting increased inter-communication, Sleeping Sickness began to extend its endemic area, especially so in the direction of the Upper Congo basin and towards the Portuguese colonies to the south of the Congo. Gradually it crept up the great river until it got as far as Stanley Falls, and now the riveraine villages over a large part of the Congo Free State, villages in which the disease was formerly unknown, are only too familiar with this terrible scourge.

Unfortunately the disease has not been contented to confine itself to West Africa. Some time about the end of the century it jumped the watershed and appeared for the first time on the eastern side of the continent, in the upper part of the Nile Valley. Gradually it has spread and is now thoroughly established in Uganda and some neighbouring countries, and threatens to move down the Nile and invade the Egyptian Soudan. This is a serious matter for Tropical Africa, and possibly for Tropical Asia, for it is difficult to say how far the area will extend. We know that in those regions to which it has already extended the mortality has been frightful. All along the shores of the northern half of Victoria Nyanza, and in the neighbouring islands, it is raging at the present moment. In parts the country has been depopulated. It is estimated that in Uganda and Busoga alone forty thousand have died of Sleeping Sickness within the last few years, and the mortality is still going on.

Becoming alarmed at the rapid progress and the appalling ravages of the disease, and apprehensive about Egypt and possibly India, the British Government, in June, 1902, got the Royal Society to send commissioners to Uganda to investigate, and if possible to find out the cause of Sleeping Sickness, with the view of instituting measures to stay its spread.

Prior to the labours of this commission many ideas, some of them manifestly untenable, had been advanced as to the cause of the disease. Only two of these hypotheses had for their basis any considerable body of fact, or could be taken at all seriously. One of these suggested that a nematode, *Filaria perstans*, was the cause; the other that a certain micro-coccus,

discovered by the members of a Portuguese commission, of which Battencour was the leader, was the responsible agent.

Filaria perstans was discovered in 1891. It was first recognised in the blood of a negro dying from Sleeping Sickness in a London hospital. The concurrence of a strange parasite and a strange disease naturally suggested a connection between them. When, subsequently, blood films sent from Africa from a considerable number of cases of the same disease were found, in practically every instance, to harbour the same parasite, the idea that there was such a connection was strengthened. Later still, two negroes suffering from Sleeping Sickness were brought to London for purposes of study; in both of them *Filaria perstans* was found in abundance. The evidence then was very strong for a cause and effect relationship between parasite and disease, more especially as, so far as inquiry had at that time extended, the geographical range of parasite and disease seemed to coincide, and as such a relationship would explain the long incubation of the disease and its non-communicability outside Africa.

On extending the inquiry to the general population of certain places where Sleeping Sickness was prevalent, it was found that a large proportion of the native negroes, whilst showing no sign whatever of being affected with Sleeping Sickness, nevertheless harboured *Filaria perstans*. The same parasite was also found among tribes unaffected with Sleeping Sickness, or only rarely affected with Sleeping Sickness. Moreover it was found in America, in British Demerara, in about sixty per cent. of the native Indians of the back country, among whom Sleeping Sickness was not at that time definitely known to be

present or absent. So far it had never been found in natives of East Africa. Co-endemicity of disease and parasite therefore could not be said to be absolute.

Soon after it became known that Sleeping Sickness had appeared in Uganda, *Filaria perstans* was sought for in the blood of the sufferers, and, sure enough, was discovered in nearly every instance. It was also found in the blood of a large proportion of the general population.

Accordingly the commissioners sent by the Royal Society were instructed to study this question of the relationship of *Filaria perstans* to Sleeping Sickness. At the commencement of their work they naturally had their attention called to the cases occurring in the neighbourhood of their laboratory and hospital at Entebbe, the seat of Government in Uganda. Here they found *Filaria perstans* in about ninety per cent. of the cases examined, a percentage of incidence considerably higher than that obtained in the general population. But when they proceeded to investigate the blood of natives in other and neighbouring districts, they found large areas in which Sleeping Sickness was prevalent but in which *Filaria perstans* was absent, and, conversely, other districts in which *Filaria perstans* abounded but in which Sleeping Sickness was absent. Manifestly, therefore, *Filaria perstans* has nothing to do with Sleeping Sickness; when the two are present in the same individual the association is merely a matter of concurrence.

The Portuguese commission referred to had found a coccus with special cultural characteristics in a large proportion of their cases. They found it in the brain and meninges associated generally with inflammatory

exudate, and they regarded it as the specific germ of the disease. One of the British Commissioners—Castellani—found the same or a similar micro-coccus in a large proportion of his cases so frequently that at one time he too regarded the bacterium as the germ-cause of Sleeping Sickness. Later, however, on finding a trypanosome in the centrifuged cerebro-spinal fluid of one, and subsequently in others of his cases, as well as in the blood, he changed his mind and put forward the trypanosome as the true cause, the coccus being regarded merely as a terminal epiphenomenon.

Colonel Bruce and subsequent commissioners confirmed and extended Castellani's discovery; and now we know that a trypanosome resembling if not identical with *Trypanosoma gambiense* has been found in the blood, in the cerebro-spinal and other serous fluids, and in the lymphatic glands of practically all cases of Sleeping Sickness which have been critically examined by competent observers.

This, undoubtedly, is good *prima facie* evidence in favour of the trypanosoma being the cause of Sleeping Sickness. But we must recollect that at one time similar evidence could have been adduced in favour of *Filaria perstans*. After all it is only evidence of concurrence. Indeed we know that some of the lower animals are the subjects of non-pathogenic or feebly pathogenic trypanosoma infections, as, for example, *Trypanosoma lewisi* in rats and *Trypanosoma brucei* in the large game of Africa. It might very well be that Sleeping Sickness depends on some altogether different germ, and that the trypanosoma found in this disease is merely an accidental concurrence; very frequent it is true, but after all only accidental and not pathogenic. And this idea was strengthened

by the discovery that a very large proportion of the apparently healthy population of Uganda, thirty per cent., harbour the parasite. On the other hand, it might be said that these thirty per cent. are in the earlier stages of the disease, and that by-and-bye they too will succumb to Sleeping Sickness as so many of their compatriots have already done. Still this must not be assumed.

Evidence was sought for in experimental inoculations of animals—monkeys particularly. Bruce infected many of these animals with trypanosomes and the monkeys sickened and died; but in one instance only has the small cell infiltration pathognomonic of Sleeping Sickness been found in their brains or elsewhere. Experimental evidence therefore, so valuable in the settlement of such questions, has in this matter, to say the least of it, been far from conclusive. A very plausible explanation of this general failure to produce meningo-encephalitis in the lower animals by *Trypanosoma gambiense* inoculations has been suggested. In the lower animals this form of trypanosomiasis usually runs a rapid course, terminating fatally before the lesion so characteristic of Sleeping Sickness has had time to develop. There may be some truth in this, for Sleeping Sickness is usually a very chronic disease, and in the only recorded case of meningo-encephalitis in the monkey the trypanosoma infection that led up to the disease ran a chronic course—over one year.

While these observations and investigations were in progress in Uganda, a very striking piece of evidence greatly in favour of the trypanosoma nature of Sleeping Sickness turned up in England. The lady to whom I have already referred as the subject of a trypanosoma infection contracted on the Upper Congo, remained under

observation in London and elsewhere. Her symptoms persisted; the parasites, although occasionally absent from the peripheral circulation, could generally be found. In October, 1903, she became completely bed-ridden. Symptoms highly suggestive of Sleeping Sickness developed, ran a rapid course, and she died on November 26th. Careful histological examination of her tissues was made by Dr. Mott, and the presence of the characteristic small cell perivascular infiltration of brain and other tissues was definitely ascertained.

The evidence afforded by this case, in conjunction with the other facts already ascertained, is almost conclusive for the trypanosoma being the cause of Sleeping Sickness. It is not absolutely so, however, for it is just possible that this lady was the subject of two concurrent infections, namely trypanosomiasis and that of what may be the still unascertained germ of Sleeping Sickness. Should other similar examples of trypanosomiasis terminating in unquestionable Sleeping Sickness occur in Europeans, and should experimenters succeed in producing the small cell perivascular infiltration by infecting some of the lower animals, preferably anthropoid apes, with cultivations of trypanosomes; and, further, should the endemic prevalence of trypanosomiasis and Sleeping Sickness on more extended investigation be found to correspond exactly, then, but not till then, although we may consider the trypanosome origin of Sleeping Sickness as highly probable, may we regard it as absolutely proved.

In dealing with newly-discovered parasites and associated pathological conditions, our experience with *Filaria perstans* should serve as a warning against precipitancy in drawing conclusions from the mere fact of concurrence.

Moreover, what we already know about some of the African trypanosomes should also make us hesitate in definitely committing ourselves to a trypanosome cause of Sleeping Sickness.

In many districts of Africa what is known as fly disease is common. If in these districts horses, dogs, sheep, in fact any domestic mammal be bitten by the fly —the tsetse fly—the bitten animal surely sickens and dies. Bruce has shown that the cause of death is a trypanosome—*Trypanosoma brucei*—very similar to that of human trypanosomiasis. The tsetse fly, acting as intermediary, carries the trypanosome from one mammal to another. But as a disease so deadly would by its very deadliness kill off all domestic mammals (and as a matter of fact and for this very reason there are no domestic mammals in the fly districts), it follows that there must be some source, other than domestic animals, from which the tsetse fly obtains its trypanosomes. This source Bruce has shown to be the wild game of the country—antelopes and so forth. These animals somehow, although not immune from trypanosoma infection, are proof against the pathogenic properties of the parasite, and so live on with the parasite in their blood, a permanent source of infection to each other, and to any other mammal entering the fly districts they frequent. This has been proved experimentally, and the results of experiments are corroborated by the long-known fact that when, by European occupation of the fly districts, the wild game of the country has been driven back or exterminated, fly disease no longer occurs among the domestic animals of the settlers.

Now, it may be that, as regards *Trypanosoma gambiense*, the negro of the endemic areas of this parasite

has acquired an immunity similar to that of the antelopes in regard to *Trypanosoma brucei*. That is to say, that in the matter of trypanosomiasis the African stands to the exotic European much in the same relationship that the wild game of his country stands to the exotic domestic mammal. The native man and beast have acquired immunity either from early infection or from inheritance, whereas the exotic man and beast have not.

There are several instances of a similar phenomenon in pathology. For example, the pyroplasma infection of cattle, known as Texas fever. As a clinical fact we know that the African does not react to trypanosoma infection in the same way as the European does, at all events he does not usually do so in the earlier stages of the infection. The febrile disturbance, so prominent a feature in the European, is often, if not generally, wanting in the African.

An important contribution towards the solution of this and other problems in connection with trypanosomiasis has been made recently by two American observers—McNeal and Novy. They have taught us how to cultivate these protozoa outside the animal body. Among other things they have shown that, as with bacterial diagnosis, the diagnostic indications supplied by cultivation of suspected blood are far more reliable than those supplied by microscopic examination alone. They have shown that in the blood of certain species of birds subject to trypanosoma infection, individual birds may often, even after prolonged microscopical examination, appear to be free from trypanosome infection, but yet, when the blood of these same individual birds is suitably cultivated, they are found to be infected.

It is also known that the blood of animals apparently microscopically free from trypanosomiasis, when injected into other and appropriate animals may give rise to microscopically recognisable trypanosomiasis, a fact often made use of in diagnosis in experimental pathology. I do not know, however, that the methods suggested by these observations have been used in the diagnosis of human trypanosomiasis.

As already stated, Bruce has shown that about thirty per cent. of the apparently healthy natives in the Sleeping Sickness districts of Uganda harbour the trypanosomes in their blood. It would be interesting to know whether the presence of the trypanosome could be shown by animal inoculation, or by McNeal and Novy's cultural methods, to exist in the balance of the population. In the case of *Trypanosoma gambiense* infection of man the blood is often, nay generally, so scantily stocked with the parasite that the organism may be hard, often impossible, to find with the microscope. But might not the more searching methods I have alluded to prove successful and show that practically all the natives of particular parts of Africa, like the big game of the country, harbour trypanosomes? Should this prove to be the case, then the trypanosome as a cause of Sleeping Sickness may have to be put out of court, just as *Filaria perstans* has been. Some other cause for the disease will then have to be sought for.

We cannot be too cautious about adopting decided views on so fundamental a matter as the etiology of a disease; everything depends on this—diagnosis, prevention, treatment. Many times we are compelled to act on conjecture or on a mere balancing of probabilities; but wherever it is possible to attain certainty, no

effort that might enable us to arrive at this should be considered too great or too costly. I consider that by systematic cultivation and injection of the blood of the natives of a Sleeping Sickness area, by the injection of anthropoid apes with cultures of *Trypanosoma gambiense*, and by systematic microscopic and cultural examination of the blood of natives outside the endemic area, we could attain absolute assurance as to whether the trypanosome is or is not the cause of Sleeping Sickness;

Glossina palpalis.

and I consider that these researches should at once be taken in hand by the governments of those countries which this terrible disease is depopulating.

However it may be as regards the relationship of the trypanosoma to the negro and to Sleeping Sickness, there can be no question as to the importance of this parasite to the European in tropical Africa. It is of practical as well as of scientific interest, therefore, to endeavour to ascertain the details of its life

history, and more especially to determine the way in which it is acquired.

Thanks to the work of Bruce on the corresponding trypanosoma of fly disease—locally known as Nagana—the carrier and mode of infection in human trypanosomiasis suggested themselves almost immediately on the discovery of the parasite. Naturally, suspicion fell on the tsetse flies. Of these there are seven species, all peculiar to Africa. *Glossina morsitans* Bruce proved

Glossina morsitans.

to be the transmitting agency in the fly disease of domestic animals. It would now appear that *Glossina palpalis* fulfils the same *rôle* as regards human trypanosomiasis. The latter insect is very common in Uganda, on the Congo, and wherever Sleeping Sickness and trypanosomiasis have been met with hitherto. It affects the wooded and jungly banks of lakes and streams, rarely, if ever, being found at a distance from water or in open country.

Whether *Glossina palpalis* be the only intermediary for the trypanosome, or whether it acts passively and simply as a mechanical carrier of the parasite on its blood-fouled jaws, or whether the trypanosome undergoes some sexual or other necessary evolutional development in the tissues of the fly, analogous to those undergone by the malaria parasite in the mosquito, have not as yet been ascertained. Most likely the *rôle* of the fly is something more than a mechanical one; for if it were not so, how comes it that we meet with trypanosomiasis only in the fly district, and not also where other blood-sucking insects occur? This is a point urgently calling for solution.

There are yet other and highly practical points demanding careful investigation. For example: Can an infected tsetse fly transmit its trypanosomes to its young, and if so, through how many generations? And again, are there other mammals besides man which, under natural conditions, harbour *Trypanosoma gambiense*, and so serve as foci of infection? The bearing of these considerations on prophylaxis is evident.

Brumpt, who travelled lately through parts of the Sleeping Sickness area of the Congo basin, has brought forward a striking piece of evidence in favour of the trypanosoma etiology of Sleeping Sickness and of the bearing of the distribution of *Glossina palpalis* in the distribution of the disease. He says, speaking of Sleeping Sickness, "In a given village it attacks more particularly those whose occupations take them to the rivers or springs—the fishermen, the boatmen, the slaves who go to fetch water, etc. One also notices that it is limited to the banks of rivers, of streams, or of shady

springs. One example which was communicated to me by the Catholic Fathers is most typical. At Banamia, close to Coquilhaville, there is a mission of Trappist Fathers situated about twenty minutes' walk from the banks of the Congo. Several years ago there was a settlement of Lolo fishermen, some three thousand in number, on the bank of the river; in 1902 barely three hundred survived; all the others had died of Sleeping Sickness. Close to the mission there is a village of agriculturists. These natives rarely go to the river, and among them, strange to say, Sleeping Sickness is almost unknown. Examples of this kind could easily be multiplied. At M'Pakou there is another mission installed at some distance from the river, but within the endemic district; the children of the mission who come from the decimated villages no longer go fishing, but become agriculturists, and rarely go to the river; among them the disease has almost entirely disappeared."

I fancy some of my hearers may be thinking I waste time in speaking at such length on diseases and conditions to which this Continent is a stranger. But, I would ask, are you quite sure that these or similar diseases do not occur in America? Until recently the fly disease of cattle was believed to be peculiar to Africa. We know now that the Surra of India and the Philippines and the Mal de Caderas of South America are also fly diseases almost identical in cause and course with that of Africa. If this be so as regards the trypanosoma diseases of the domestic mammals, may there not be a similar and corresponding trypanosoma disease of the American man, and that somewhere among the wild tribes of the Orinoco or Amazon such a condition occurs? And as in Africa the advance of

civilisation has brought about a mingling of formerly isolated tribes, with corresponding interchange of formerly narrowly-restricted disease germs, so it may be, when the time comes for civilisation to agitate these tribes of the American tropical wilderness, that similar extensions of at present limited diseases will occur, and among these a trypanosoma disease, perhaps Sleeping Sickness itself.

VI.

Febrile Tropical Spleno-megaly (Kala-Azar).

As regards the etiology of tropical disease, an interesting and instructive comparison might be instituted between the views of to-day and those that obtained say fifty years ago. In the middle of last century, with the exception of Yellow Fever and perhaps of Dengue, all tropical fevers were relegated to Malaria. So much so, that in those by-gone days when a patient suffering from fever returned home from the tropics his fever was almost sure to be diagnosed as malarial.

By degrees, however, since the use of the clinical thermometer became general and, more especially, since the rise of the germ theory of disease, and the general application of the microscope in diagnosis, the views of clinicians and pathologists have undergone a very great change. We now know that besides malaria there are many other specifically distinct febrile diseases in the tropics. One after another there have been hewn out, as it were, and definitely separated from the malarial group such diseases as Mediterranean fever, Tropical typhoid, Elephantoid fever, Trypanosoma fever, Spirillum fever, and lastly and most recently the disease about which I now propose to make a few remarks and which may be designated Tropical Febrile Spleno-megaly, or

perhaps, and more conveniently, Kala-Azar, the name it is known by in Assam, one of its principal haunts.

Those who have much experience in tropical practice come across from time to time a type of case characterised by enlargement of the spleen and liver, anæmia, recurring or more or less chronic fever, and, after several months or it may be one or two years, a fatal issue. Formerly these cases were diagnosed and treated as malarial cachexia. Probably in a proportion of these cases this diagnosis was correct, for undoubtedly splenic and hepatic enlargement, a liability to low fever, anæmia, and chronic visceral degenerations is one of the legacies of repeated malarial infection; but in many instances the diagnosis of malaria, and therefore the treatment based on this diagnosis, were both wrong.

In these latter cases the patient gives a history of tropical or sub-tropical residence, and very often of residence in a highly malarious district in which similar cases are not uncommon. He will tell that without obvious reason he was attacked with what he called malarial fever; malarial, he will explain, inasmuch as the daily paroxysms were preceded by chills and followed by profuse sweating, and recurred approximately about the same hour every afternoon, and that his medical attendant diagnosed them malarial, and treated them with quinine. After a variable period of a fortnight, more or less, he will tell us the spell of fever fits subsided to be followed by a considerable period of apyrexia, relative or absolute. Then another period of malaria-like paroxysms supervened, lasted for a week or two, again to subside; and so on for an indefinite number of weeks or months.

Shortly after the commencement of the disease, the spleen and liver began to enlarge, both organs, but es-

pecially the former, gradually attaining very large dimensions. Anæmia, languor, breathlessness, and the entire group of symptoms appertaining to imperfect blood supply soon became prominent features, persisting, together with the fever, in defiance of treatment with quinine, arsenic, iron or other drugs.

In another type of case the history given is that of a prolonged quotidian fever. Every day there is the afternoon rigor, rise of temperature to 102° Fahr. or 103° Fahr. and the terminal sweat. I possess a chart of such a case in which this quotidian fever continued with the utmost regularity for many months, and until the death of the patient from inanition. In these cases also there is the pronounced splenic and hepatic enlargement and the profound anæmia.

In yet another type the febrile disturbances are much more irregular. For days the temperature may remain normal, or there may be a rise of only one or two degrees. Then there may be a gradual rise, step-like in character, during several days to a maximum of 103° or 104°, and then a corresponding gradual step-like fall to normal. Or there may be suddenly interpolated in the course of a low irregular chronic fever an acute pyrexial attack.

The febrile manifestations are exceedingly varied, but in nearly all cases—the exceptions are rare—no matter what the type of fever may be the spleen and liver are enlarged, the anæmia is pronounced, the physical weakness is marked, and there is generally progressive emaciation; so that the penultimate clinical outcome is the production of a big-bellied, emaciated, sallow, dirty skinned, anæmic, fever-stricken patient, often bedridden, and always quite incapable of any work involving continued effort whether of body or of mind.

In going into the history of these cases, at all events in Europeans, you will generally be told that quinine has been freely administered but without the slightest benefit; that arsenic has been tried with practically similar results; and that, despairing of recovery in the hot malarious district in which the disease was contracted, after months of suffering and drugging the patient has come home being told, and doubtless believing, that the change will cure him. Unfortunately, in my experience, these hopes are never realised. Such cases, so far as I have seen, all die.

Until taught by experience, the physician is apt to give a favourable prognosis. It is true the patient has a big spleen and a big liver and some fever; but, strange to say, and this I regard as a mark of considerable diagnostic value, his tongue is clean, his appetite in spite of the fever—so different from what obtains in malarial cases—is good, he may digest his food well, there are no bilious and no threatening symptoms discoverable. Nevertheless, in spite of quinine, in spite of aperients, in spite of tonics, in spite of change, in spite of the many therapeutic measures friends and physicians suggest, the case goes slowly to the bad, and the patient, after a few months or even a year or two at home, dies either of sheer inanition or of some intercurrent infection, such as pneumonia or dysentery, to which his debility renders him extremely liable, and to which he readily succumbs. Very often before the end there may be hæmorrhages from the gums or nose, or hæmorrhagic effusions under the skin or, it may be, into the fundus oculi.

Having seen a number of these cases in China, and as returned invalids from India, Africa, and elsewhere in the tropics, I had come to regard them as belonging to a

distinct and definite pathological group altogether independent of malaria. I believed that they depended on a special germ; and, having regard to the type of fever, the anæmia, the enlargement of the spleen, the non-amenability to quinine, the complete absence of the malaria parasite, after the discovery of the *Trypanosoma gambiense* as a human parasite I hazarded the conjecture that the germ at the bottom of this tropical febrile splenomegaly was a trypanosome also, or at all events a similar parasite.

I endeavoured to link up these cases with a disease known in India under the name of Kala-Azar, a disease which for a good many years had puzzled the profession as well as the Government in that country. Kala-Azar exhibits exactly the same combination of symptoms, and runs exactly the same course, as the cases of splenomegaly I have attempted to describe; and, moreover, the native name Kala-Azar—Black Fever—indicates another point of agreement; for the name is given in allusion to an occasional but by no means invariable symptom, namely, pigmentation of the skin, which I have seen in at least one European case from India. About 1887 a chronic and very fatal form of febrile disease, which received from the natives the name I have just mentioned—Kala-Azar—appeared in epidemic form in Southern Assam. Gradually spreading along the lines of communication and clinging for the most part to the cultivated valleys, it extended over a large part of the country. The consequent mortality in some districts has been enormous. Entire families were wiped out. Villages were decimated, and a considerable proportion of the cultivated lands fell back into jungle. The population of the areas involved, which under British rule had

for years shown a gratifying increase, began to decrease. The State revenues also were materially affected.

The disease crept slowly from village to village at an average rate, it was estimated, of about five miles a year. It was observed that the earliest cases in a hitherto unaffected village could nearly always be traced to someone suffering from the disease who had come from an already infected locality. This imported case became a focus from which the disease spread, first to the inmates of the house in which he lived, and subsequently to the rest of the village. The natives from a repetition of such experiences came to regard Kala-Azar as infectious, and in some instances in which this view was adequately acted on, and strict isolation maintained, the disease did not spread. It was further observed in the infected villages, that after a period of years—five or six—the virulence of the disease, or rather its infectivity, seemed to abate, cases cropping up only sporadically. Thus, like some huge serpiginous ulcer, Kala-Azar has been slowly advancing over Assam, leaving in its track permanent reminders, in the shape of sporadic cases, of the decimating epidemic that is sweeping over the land. The virulent epidemic passes on after establishing, so to speak, a permanent though less infective endemic.

In passing I might remark that in this circumstance this fizzling out of a devastating epidemic into a relatively unimportant endemic, considering, as I shall presently point out, the similarity of the germ causes concerned, there may be an element of hope for Uganda, which, as described in my last lecture, appears to be on the verge of absolute depopulation by Sleeping Sickness.

Commissioners have been sent to Assam at various times by the Indian Government to study Kala-Azar, and

to make suggestions as to the treatment of the disease and the control of the epidemic. One commissioner regarded it as Ankylostomiasis plus malaria; another as a virulent type of malaria; a third as malaria with a super-imposed secondary infection. None of the measures or suggestions founded on these theories appear to have exercised any beneficial influence, either as regards the treatment of particular cases, or as regards arrest of the epidemic.

Such, until quite recently, was the position of affairs as regards Kala-Azar or tropical febrile spleno-megaly. Some regarded it as a form of malaria, others regarded it as a disease sui generis. Nothing of a positive character was known as to its actual nature, as to its treatment or prevention, and the mortality continued practically uncontrolled.

In the winter of 1902–3, Major Leishman, of the British Army Medical Service, observed in smears of blood and internal organs of a trypanosoma-infected rat, about forty-eight hours after death, a number of minute spherical or oval bodies possessing features extremely suggestive of a close relationship to the trypanosomes with which they were associated.

A trypanosome successfully stained by the Romanowsky method presents two well-marked chromatin masses. One, the larger, is located about the middle of the creature's body; the other, very minute, but very deeply staining, is situated close to the posterior or non-flagellated end. The former is the nucleus; the latter is variously termed micro-nucleus, chromosome, centrosome, etc. Now, the spherical or oval bodies found by Leishman in the spleen of the rat possessed two such chromatin masses —a very minute and deeply staining one, and a larger

and less deeply staining one; features which, taken together with the fact that the bodies exhibiting them concurred with an undoubted trypanosoma infection, suggested to his mind that these oval or spherical bodies represented a phase in the post-mortem evolution of a flagellate.

Some years previously—to be accurate, November, 1900—the same observer had encountered similar bodies in smearings from the spleen of a soldier who had been invalided from India and who had died in the military hospital at Netley. The man had succumbed to what is known in Indian medical circles as Dum Dum Fever, in other words the type of disease I have just described.

Leishman body. (*From a photo by Mr. H. Spitta.*)

Dum Dum is a military station not far from Calcutta, and has gained an unenviable notoriety for this type of what was formerly supposed to be malaria. Leishman published the observation in the *British Medical Journal* of May 30th, 1903, and suggested that the bodies in question, in view of their anatomical features, and what he had recently seen in rats, were of the nature of trypanosomes, possibly allied to *Trypanosoma gambiense* —a parasite which was exciting a good deal of attention, having been discovered only a short time before.

Somewhat later similar "Leishman bodies," as they are now called, were found by Professor S. Marchand, of Leipsic, in sections of the bone marrow, spleen, and liver of a German soldier who died of a febrile splenomegaly acquired apparently during the recent Pekin campaign.

Soon after Leishman announced his discovery, Donovan obtained the parasites by splenic puncture

from natives of India; later, Low and myself obtained them from a European patient invalided from that country. Since then the Leishman body has been found in natives of the Egyptian Soudan and of Algiers. More recently James, Bentley, Rogers, and others have found it in natives of Assam suffering from typical Kala-Azar; and still more recently Dr. Airde has found it in Hankow, China, where apparently febrile spleno-megaly is far from being uncommon.

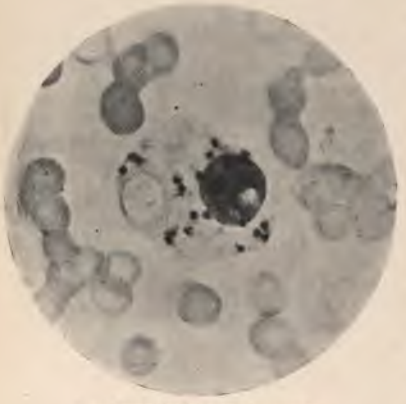
Leishman body.
(From a photo by Mr. H. Spitta.)

Thus, within the last two years, a new disease has been added to the long list of the ills that flesh is heir to, and another large group of cases has been definitely removed from the mass of disease attributed to malaria.

Although, so far, we have not heard of tropical spleno-megaly in America, this disease has undoubtedly a wide range in the tropical and sub-tropical zone, and may very well occur in the warmer parts of the Western Hemisphere; or, if not already present there, may be subsequently introduced. Its clinical characters, although misinterpreted, have long been known, and known in many places. Sporadic cases occur pretty well all over India. In some places, as Madras and Dum Dum, they are fairly numerous; in other places they are rare; in one or two places, Assam for example, the disease, as already mentioned, rages as an epidemic. So

that we now know that the "Leishman body" is an important and very grave factor in tropical pathology.

If the spleen or liver of a patient suffering from tropical spleno-megaly be punctured with a fine exploring needle, and a little of the pulp, or pulp mixed with blood, of either of these organs be aspirated into the barrel of the needle, and subsequently blown out and spread as a film on a microscope slip, and if the film so prepared be stained by the Romanowsky method, the following objects will be recognisable under high powers, and generally in great profusion:—



Leishman bodies in phagocyte.
(*From a photo by Mr. H. Spitta.*)

(*a*) Minute oat-shaped, oval or spherical bodies, faintly stained as regards their protoplasm, but exhibiting, as already described, very definite deeply staining chromatin masses, usually placed at opposite ends of the shorter diameter of the little bodies. Of these chromatin bodies one is relatively large, oval or spherical in shape, and stains less deeply than the other very much smaller and generally rod-shaped body. These are the Leishman bodies.

(*b*) Similar bodies in groups of two to fifty, or even more, closely set in a faintly-staining amorphous matrix in many instances of an absolutely regular discoid or spherical shape.

(*c*) Scattered groups of Leishman bodies mixed up with fragments of the matrix just mentioned, the disposition of the bodies and fragmented matrix suggesting that the group was originally one of the spherical or discoid masses just described, which had been broken up in the spreading of the film.

(*d*) Leishman bodies enclosed in, but in no sense disintegrated or acted on by macrophages.

When the patient dies the post-mortem reveals, in addition to such superposed conditions as dysentery or pneumonia, which may have been the immediate cause of death, an enlarged—usually enormously enlarged—red, firm, friable spleen, and an enlarged, firm, tough liver. Microscopical examination of these organs and of the bone marrow discloses a prodigious amount of parasitic invasion. In the bone marrow and in the spleen there may be more infected than healthy cells. One wonders in contemplating the sections how the patient could have lived so long as he did, so abundant are the parasites. In spleen and bone marrow every type of cell seems to be invaded. In the liver it is otherwise; here the parasite occurs principally in the endothelial cells of the capillaries and lymphatic spaces; the hepatic cells, though often extensively degenerated, are not invaded by the parasite.

Although these three organs are the principal seats of the parasite, other organs, and even morbid effusions and structures are not spared. Thus Leishman bodies may be found in the lymphatic glands, the supra-renal capsules, testes, pleuritic exudates, and other inflammatory effusions especially—and this is a point I shall return to—the bases of ulcers both intestinal and cutaneous.

I have mentioned that in smears of spleen pulp obtained by splenic puncture during life sharply defined

spherical or discoid masses of a homogeneous material crowded with Leishman bodies often occur. Such masses vary in size from half the diameter to bodies three or four times the diameter of a red blood corpuscle. So regular in outline are they that Laveran seems to have been deceived into mistaking the smaller of them for red blood corpuscles. They have no nucleus. What may these circular bodies be? Christophers believes that they are the remains of tissue cells in which the parasites had developed, and which had been killed by the parasites. This suggestion, although it may account for the absence of nucleus, does not explain the accurately circular shape of many of these masses, nor their clearly defined outline. Strange to say, these circular or spherical masses are not apparent in sections of the diseased organs.

A striking and, from the point of view of curability of the disease, discouraging fact is that whereas the invaded cell often shows signs of degeneration, there is no indication that the including cell exercises any destructive influence on the parasite. In many instances the staining reaction of the invaded cells is normal, as if between the cells and the parasite a comfortable symbiosis had been established.

On contemplating the prodigious profusion of parasitic growth in the spleen, liver, and bone marrow, one readily understands the fatality and hopelessness of this disease. Personally, I have never seen a case of tropical spleno-megaly recover. It is true my experience is a limited one, but Rogers, who spent months in the most affected districts of Assam, states the case mortality at about 96 per cent. Donovan likewise regards the disease as almost necessarily fatal. I fear this view, until some

treatment more efficient than any we yet possess is discovered, must be regarded as near the truth.

By what channel does the Leishman parasite leave the human body? What happens to it during its passage from human body to human body? How is it acquired? How does it multiply when acquired? What is its zoological status? These are important questions. On our ability to answer some of them will depend our power over this disease, a disease quite as terrible as and, in its epidemic and endemic behaviour, singularly like the Sleeping Sickness.

How does the Leishman body escape from the human host? Does it escape in the secretions? It has not been found in any of these.

Is it removed from the blood by some insect as in the case of the parasite of malaria, of filariasis, of yellow fever, and probably of Sleeping Sickness? Towards the termination of severe cases of spleno-megaly, Christophers has found it in considerable numbers in the white blood corpuscles. This, however, is very unusual; Leishman's body is rarely found in the blood. In the course of prolonged systematic search at the London School of Tropical Medicine in a typical case it was not once found in the blood. This rarity tells against the blood as being the normal channel of escape. Possibly, as with the virus of yellow-fever, it may have an ultra-microscopic blood phase in which it effects its escape. There are facts, though not conclusive, against such a supposition, facts which I shall mention presently.

The selection by the parasite of such organs as the spleen and bone marrow suggests, indeed, an intimate connection with the blood; and in addition to this there are other facts that favour the idea that, although the

parasite does not escape directly in the blood, the blood stream is the route by which it is carried to the point of escape.

So far the evidence favours the idea that the Leishman body effects its escape in the morbid discharges from intestinal and integumental ulcerations and similar lesions.

As already mentioned, the bodies have been found by several observers in the granulation tissue of intestinal ulcers. It is a significant fact that the majority of Kala-Azar patients die of dysentery, or of some similar form of intestinal flux associated with ulceration.

And here comes in, I believe, the peculiar significance of the recent remarkable discovery, or rather re-discovery, by the American observer, Wright, that the chronic form of ulceration known as Oriental Sore is associated with the presence in the morbid tissues of bodies morphologically identical with the Leishman body.

Many years ago—1885—Cunningham, and later—1901—Firth described certain minute bodies in the protoplasm of the small cell exudate constituting the base of the Oriental Sore. They regarded these bodies as parasitic in their nature; in fact Firth alluded to them as *Sporozoa furunculosa*. At that time chromatin staining had not been carried to its present state of perfection, and the importance of the observation was missed until Wright, using the Romanowsky method, gave it the prominence it deserves. Lately it has been further shown that the typical Oriental Sore is not the only type of skin lesion in which these or similar parasites occur, for they have been found in the exudation cells of innocent-looking pustules, and even in the serous contents of the highly contagious bullous skin affection common in the tropics and known as pemphigus contagiosus.

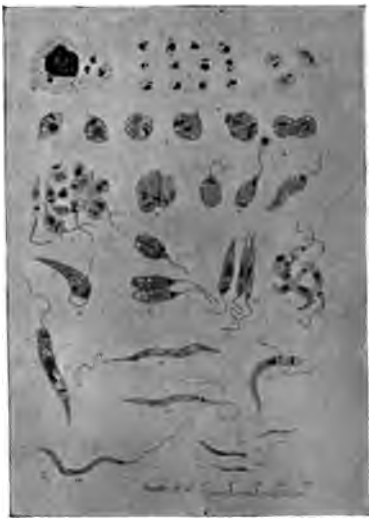
The occurrence of the parasite in ulcerating surfaces, and the frequency of ulceration in this disease, suggest that the ulcerating surface is the door by which the parasite leaves the human body; and the occasional presence of the organism in the white blood corpuscles further suggests that they are carried to the point of escape by the blood from the great germ stores in the spleen and bone marrow.

What happens to the Leishman body in its passage from human body to human body? What is its zoological status? Although the Leishman body has been discovered only very recently we are already in a position to give a partial answer to these questions. Capt. Leonard Rogers, of the Indian Medical Service, has shown, and his observations have been confirmed by Leishman himself and also by Christophers, that if infected blood or spleen pulp be mixed with citrate of soda solution, and kept at a temperature considerably below that of the human body, namely, at 22° Cent., the parasites multiply, increase in size, and ultimately develop into flagellated organisms, long, slender and motile like a trypanosome. They differ, however, from the ordinary type of trypanosome, inasmuch as the flagellum springs directly from that end of the body at which the micro-nucleus is situated, and is not prolonged forwards to the other extremity, or united to the body of the organism by any structure resembling a swimming membrane.

This is an important discovery, for it indicates that the first step in the extra-corporeal life of the parasite is made in a cold medium—either dead or living, in soil or water, or in the body of a cold-blooded animal. Most probably the latter; for the next step, the introduction of the parasite into the human host, has to be provided

for, and the method of introduction is suggested not only by what we know of other similar parasites, but also by what we know of the usual location of Oriental Sore in the human body.

Now this peculiar type of ulcer occurs in the great majority of cases on the hands, fore-arms, or face—that is to say, the uncovered parts of the body—those most exposed to the attacks of biting insects. I would suggest, therefore, that the Leishman parasite leaves the human body in the discharges from ulcerated surfaces—intestinal or cutaneous; that it is ingested by some foul feeding fly; that in this intermediary it undergoes evolutionary changes and probably multiplication, perhaps of a sexual nature; that it is then implanted into the human host by this insect by bite or contact with broken skin surface; and that in the human host, as can be readily shown, it multiplies by division and probably asexually.



Development of Leishman body.
(*After Leishman.*)

This hypothesis is plausible enough; not for unqualified acceptance, but to justify further work in the endeavour to confute or establish it. If established, its practical bearing on the management of cases and on prophylaxis is evident. At the outset of any such attempt we are brought up by the incontrovertible fact

that, although the Leishman body is intimately associated with tropical spleno-megaly, a fatal disease, it is also intimately associated with Oriental Sore, an absolutely benign diease. In the latter disease there is no spleno-megaly, no constitutional disturbance, no general invasion by the parasite. Tropical Sore is not followed by spleno-megaly, so far as we know. If the opposite were the case the outlook for Europeans in India, and even for the entire population, native and foreign, in such places as Bagdad, would be bad indeed. In Bagdad, and in many other Oriental cities, nearly everyone after a few months' residence gets Oriental Sore.

Herein lies a most interesting problem. Is the Leishman body of Oriental Sore identical specifically with that of spleno-megaly? If specifically identical, as it undoubtedly is morphologically identical, how is it that the innumerable subjects of Oriental Sore do not get spleno-megaly and die? I once, but only once, saw a constitutional infection, or what I took to be constitutional infection, follow Oriental Sore. In this case the testes became enlarged and indurated by what was believed at the time to be tubercular disease. Whether this was Leishman body infection or tuberculosis I cannot say, as the testes after excision were not examined microscopically. This is the only instance, if instance it be, in my experience of anything like constitutional involvement by Leishman body infection. Even if it were a true example of constitutional invasion it is quite exceptional, and for all practical purposes may be disregarded.

There is a curious fact about Tropical Sore which, to my mind, is highly suggestive. Tropical Sore is a very chronic affair; it generally lasts for many months, sometimes for a year, or even longer. But when it has

healed thoroughly it does not recur, and the subject of it usually enjoys immunity, I believe, for the remainder of his life. A second attack is distinctly unusual. The Bagdad Jews know this, and formerly, I believe, they acted on this knowledge with the object of preventing the disfigurement of their female children by the unsightly scarring of the features so often resulting from the healing of the Bagdad boil—to give Oriental Sore its local name. These Jews used to inoculate their children on some convenient part of the body covered by the clothes, thereby anticipating the spontaneous development of the sore on some exposed and undesirable part of the body—face or hands. In this way immunity was established and unsightly scarring prevented.

It has been remarked that Oriental Sore is a disease peculiar to camel-using countries. I cannot vouch for the accuracy of the observation, but those who advance it would have us infer that somehow the disease is contracted from camels, much in the same way that vaccinia is contracted from bovines.

Now, if the Leishman body of Oriental Sore be specifically identical with the Leishman body of tropical spleno-megaly, it must somehow have been deprived of its virulence; and I would suggest that this reduction of virulence has been effected by passage through the camel, just in the same way as the virus of smallpox is deprived of its virulence by passage through the cow. If the vaccinia virus protects against smallpox, may it not be that Oriental Sore virus would protect against tropical spleno-megaly, against Kala-Azar? I commend the idea to those who have an opportunity of testing it experimentally.

VII.

The Diagnosis of Tropical Fevers.

In the foregoing lectures I have endeavoured to indicate the principal factors that determine the occurrence and geographical limitations of tropical diseases. I have shown that these factors have nothing to do with any special condition of the human body that may have been determined by climate, but that they are exclusively concerned with the necessities of the disease germ in its passage from one human body to another. I have also endeavoured to illustrate this cardinal principle in tropical pathology and its bearing on treatment and prevention, and, in the case of a number of diseases, especially in the case of the more recently separated tropical diseases, have entered into considerable detail.

Perhaps some of my audience may think that such a mode of treating my subject is not altogether a very useful or a very practical one. I entirely differ from such an opinion; for science, that is knowledge, accurate knowledge of facts and the principles co-ordinating facts, is the only sound basis on which to build practice and progress.

In this and the two succeeding lectures I propose to change somewhat my method of dealing with my subject. I propose to treat it from the clinical standpoint,

endeavouring, where available, to utilise the findings of pathological science to help us in diagnosis and to guide us in practice.

And here again, in consequence of the magnitude of the field, I must put on myself certain limitations. I have therefore selected two or three subjects about which to speak, being influenced in my choice by what I imagine will possess most interest and prove of most value to my hearers.

In temperate climates the clinical conditions of tropical origin with which the practitioner is most frequently called upon to deal are, first, fever, and second, intestinal flux.

The interpretation of these symptoms, for they are only symptoms, and the management of the diseases on which they depend, I propose now to consider.

Judging from my personal experience of tropical practice in London, about half of your tropical patients here in San Francisco will consult you about fever. In almost every instance the patients will come with a diagnosis already made. They will tell you they are suffering from "malaria."

A patient reasons in this way: "I have been in the tropics. Malarial Fever is the disease *par excellence* of the tropics. I have got fever; therefore I have got Malarial Fever."

Now, speaking from a large experience, I feel fairly confident in affirming that in the vast majority of cases this diagnosis will prove to be wrong. It is true that most people who reside in the tropics for any length of time sooner or later contract malaria; but it is equally true that they do not acquire immunity from other fevers, or from other diseases of which fever

is an accompaniment. They are just as liable as those who stay at home—perhaps more liable—to ordinary febrile diseases. And, in addition, they are exposed to other chronic affections peculiar to the tropics, of which fever is often a prominent symptom. Therefore, in dealing with febrile complaints in such patients, I advise you to ignore absolutely the diagnosis the patients volunteer, and, for that matter, the diagnosis supplied by inexperienced physicians. Accept no man's diagnosis unquestioningly.

To emphasize this point I would again repeat that the probabilities are that a diagnosis of malaria volunteered by a patient or suggested by an inexperienced practitioner in a tropical case is, in the majority of instances, wrong. The reason for this is not far to seek. Everyone knows that quinine cures malaria. Therefore when a man gets malaria he generally takes quinine. It is principally those cases of fever which have resisted quinine—that is, the non-malarial cases, that you will be consulted about. The malarial cases will have cured themselves or have been cured by the doctor, and the consultant does not get a chance at them; at all events not nearly so often as he does at the non-malarial fevers—that is, the fevers which have resisted quinine.

In attempting the diagnosis of a chronic or recurring fever whose nature is not at once apparent, I would urge you to disabuse your mind not only of the idea that the fever is malarial, but also of the idea that it is necessarily tropical. Put the idea of malaria and the tropics out of your mind altogether. Look on the patient in the first instance as an ordinary one who has never been abroad. Search systematically

organ after organ for an explanation of the symptoms, never losing sight of those great pandemic diseases, tuberculosis, syphilis, typhoid.

Inquire in some orderly, all-embracing method for indications of middle-ear disease, of suppuration in the antrum, in the frontal sinuses and upper air passages. Examine the lungs carefully for tubercle, for dilated bronchus, for pleural effusion, for empyema. Do not overlook the possibility of ulcerative endocarditis or of pericarditis. Examine the liver for abscess, for suppurating hydatids, for gall stones, for inflammation of the gall bladder. Think about subphrenic abscess, chronic peritonitis, appendicitis, splenic leucocythemia; palpate the kidneys carefully, and search the urine for pus as evidence of pyelitis, stricture, urinary abscess. Do not overlook the ovaries, or the possibility of pelvic cellulitis, or of fistula. See that there is no tenderness or deformity of the vertebræ or of other bones. In other words, go over the organs one after the other on the outlook for pus, for tubercle, for syphilis, for typhoid, and the hundred and one diseases which flesh is heir to.

If this search prove in vain, then, but not till then, you may think that possibly you are dealing with a tropical case. Arrive by careful exclusion at this view. Then put to yourself the question, "What are the tropical diseases that are or may be attended with chronic or recurring fever?" Go over them in your mind and see if your patient's case conforms to one or other of them.

Most acute tropical diseases you may disregard; for, by the time such a case could have reached the temperate zone, the disease has run its course, and the patient is either dead or recovered. The causes of chronic or

recurring fever, therefore, are those with which you have to deal.

The principal of these, I mean such of them as you will meet here in patients from the tropics, are as follows:—

(1). Malaria.
(2). Mediterranean Fever.
(3). Liver Abscess.
(4). Elephantoid Fever.
(5). Trypanosomiasis.
(6). Tropical Spleno-megaly or Kala-Azar.
(7). Relapsing Fever.
(8). Leprosy.

Inasmuch as malaria is an exceedingly common disease in the tropics, and as the question of malaria is sure to crop up in discussing any difficult diagnosis, it behoves you to be able to recognise without fail this infection, and to pronounce positively as to whether any given febrile condition is malarial or is not malarial.

Fortunately, we are able to do this with precision; that is, provided we set about the diagnosis in a systematic and scientific way. On these conditions there is no disease so surely recognisable as malaria.

There are three absolutely diagnostic tests for this infection, one, or other, or all of which can be applied successfully in most cases. We have a clinical test—periodicity; a microscopical test—the presence of the parasite or of its products in the blood; and a therapeutical test—the reaction of the disease to quinine.

First—periodicity. Any febrile complaint with a definite tertian or quartan periodicity is certainly malarial. No other infection exhibits this type of periodicity.

You may be sure then that a patient complaining of fever recurring every forty-eight or seventy-two hours, whatever else he may have, certainly has malarial disease.

Although the cycle of the parasites causing malarial disease is one of forty-eight hours, or one of seventy-two hours, owing to infection by two or three generations of parasites many malarial agues and fevers exhibit a periodicity which, clinically, is quotidian. It is not right, therefore, to infer that because a fever is quotidian it is not malaria. Unfortunately, it is even more incorrect to infer, as is so often done, that because a fever is quotidian and is attended with ague-like symptoms—rigor, elevation of temperature, sweating, it is necessarily malarial. Thus quotidian periodicity becomes a trap to the diagnostician; a trap into which many have fallen, sometimes with disastrous results. Quotidian periodicity is more misleading than guiding. Therefore, let me say it emphatically, quotidian periodicity should be absolutely ignored as an indication of malaria.

Often we are consulted by patients from the tropics for quotidian fever. They point to a temperature chart showing a definite quotidian periodicity. They tell a story of constantly recurring afternoon rigor, followed by high temperature, profuse night sweats, and complete apyrexia during the earlier part of the day. Thus backed, and coming from the tropics, and possibly having suffered from malarial fever there, they tell you that their complaint is certainly malaria. Now most of these patients have arrived at this diagnosis weeks perhaps before you see them. They have taken large doses of quinine. Probably it is because these large doses of quinine have failed to check the fever that you are

consulted. As a matter of fact, in such cases you are consulted not about diagnosis; you are consulted about treatment. The patient wishes you to prescribe for him anti-malarial remedies other than and better than the quinine he has been taking.

As I shall point out presently, quinine properly administered and in adequate doses never fails to check, or modify at least, a malarial attack. This much, therefore, you may be quite sure about. Patients exhibiting this type of quotidian fever and who have taken quinine thus freely are not suffering from malarial fever. The diagnosis is wrong.

Don't overlook the fact that in nearly all pathological processes attended with fever, no matter what its cause, quotidian periodicity, more or less pronounced, may be observed in the recurrences of the fever. Tuberculosis, syphilis, abscess, and many specific fevers have invariably, or nearly invariably, an afternoon rise of temperature which, in many of them, is preceded by ague-like chilliness and followed by profuse diaphoresis.

Perhaps in consequence of the periodic quotidian fever usually accompanying it, the tropical disease most frequently confounded with malaria is Liver Abscess. It is quite a common occurrence to be consulted by patients affected with grave suppuration of the liver, who for weeks or even months have been under the impression that their disease is malaria, and who, in fact, have been treating themselves for malarial disease. I think it is Osler who has said that he had never seen a case of Liver Abscess that had not been drenched with quinine. I could tell many stories illustrative of this.

Some years ago I was asked by a lady to see her husband. She told me that he had been invalided from

India on account of malarial fever; that he had been in England for several months, and that all this time the fever had continued; that he had taken quinine persistently and in liberal doses; that he was gradually getting worse; and that he had become a confirmed invalid and was confined to bed. On visiting the patient, who was himself a physician, he too volunteered the diagnosis of malaria. He said his object in asking me to see him was to get me to make an examination of his blood for the malarial parasite. When he informed me of the liberal dosing with quinine to which he had subjected himself I told him, without further question or examination, that I was sure he was not suffering from malaria; that had this been the case the quinine he had already taken would have cured him long ago. I further told him that it was no use to make an examination of the blood for the malarial parasite whilst he was under the influence of this drug. On inquiry, I found that shortly before the fever began, and while in India, he suffered from a slight diarrhœa which to him seemed to have been of a dysenteric nature. It had lasted for a few days only and had not recurred. On this apparently trifling intestinal flux the fever had gradually supervened. On examining him, instead of finding the spleen enlarged, as one would expect after so prolonged a course of malarial fever, the organ was not palpable. On the other hand, the liver was very much enlarged, although not tender. It was evident that he was suffering from a deep-seated abscess of the liver, and not from malarial fever. I told him so; but he pointed to the temperature chart which by this time had attained a length of several yards, to the typical quotidian afternoon rise of temperature to 103° Fahr., or thereby, duly

chronicled day by day. He dwelt on the regular occurrence of afternoon rigor and evening sweats, and he persisted in maintaining that his diagnosis of malaria was correct. To please him I said I would examine his blood on condition that he left off quinine for a week. He did so, and at the end of the week the patient being neither better nor worse for the omission of the drug, I examined the blood and found no trace whatever of malarial parasite. Again I urged my diagnosis of liver abscess and the necessity for exploration. He refused and demanded bigger doses of quinine. These he had for another week. Still there was no reduction of the evening temperature. Finally, I persuaded him to submit to the exploration of the liver, with the result that a large abscess was found and successfully drained. This is typical of a set of cases with which those of us accustomed to tropical practice are only too familiar.

About the same time I was asked to see another Indian physician said to be suffering from malarial fever. When I got to the house I found the patient moribund. From his wife's story I felt fairly confident that the case was not malarial. The patient being unconscious I did not have his assistance in my endeavour to locate the pus which I assumed to be at the bottom of the symptoms. While attempting to get facts likely to help me I looked round the room. I came upon an old and rotten catheter. This supplied the necessary hint. I examined the patient's perinæum and there found an extensive swelling. A free incision gave vent to a large quantity of pus and urine. The man was dying not from malaria but from urinary abscess, the result of stricture. Judging from the fact that treatment with quinine had been energetically carried out and persevered

in for a considerable time, it was evident that both the patient and his wife had been under the impression that the fever symptomatic of the perineal abscess was malarial in nature.

Some time ago I was asked to see a gentleman who had been travelling in Mexico. He told me that when in Mexico City he was suddenly seized with fever attended by rigor and sweatings. Similar attacks recurred regularly every day for a week. He was treated with quinine and for the time being recovered. On his way home he had a series of attacks in New York; these, too, had been treated with quinine. Subsequent to his return to England he had several similar spells of quotidian fever. I was consulted with the idea that possibly something other than malaria might be responsible for the recurring fever spells. At all events I was consulted on the question of malaria. On careful inquiry I learned that the patient had not been in a malarial country during the malaria season. The inference from this, and from the fact that the persistent use of quinine had no effect either in preventing or in cutting short the attacks, was that he certainly could not have malaria. An examination of the blood confirmed this opinion. There was no enlargement of the spleen. On the other hand there was a history of renal calculus, and there was also a history of trouble in the region of the gall bladder. At the time of my examination there was no evidence of renal trouble, but there was some tenderness about the gall bladder. Ultimately the gall bladder was cut down on and found to contain pus. It was drained, and the patient made an excellent recovery.

I was asked to see a young gentleman who was suffering from a quotidian fever of considerable standing—

about two months, if I recollect aright. He had been seen by many of the leading physicians in London. Some thought he had one disease, some that he had another disease, and there had been a corresponding diversity of treatment. Still the disease held on. The patient had been to Rome; and as Rome has an evil reputation with some people for malaria, although the visit had not been made during the fever season it was thought that possibly the patient was suffering from malaria. I was asked to pronounce on this point. As quinine had had no restraining influence on the fever, and as I could find no evidence of malaria in the blood, I negatived the suspicion of malaria; but I could find no adequate ground for a definite diagnosis, and said so. Some weeks afterwards I met a friend in the street —a friend who specialises in ear, nose, and throat—and in the course of conversation he said, "By the way, you saw so and so," mentioning the patient's name. "Yes," I said, "is he dead?" "No," was the reply, "far from it. Soon after your visit he complained of a feeling of stuffiness in the nose, and I was sent for. I could find nothing wrong; but with the view to preparing the patient for a more complete examination I prescribed an alkaline nasal douche. Next day when I visited him to make the proposed examination I was told that there had been no return of fever the previous afternoon, and that the patient felt quite well. There was no subsequent return of fever, and the patient is now in good health." In this case there must have been pent-up pus in some of the nasal passages or accessory cavities. The alkaline douche had removed the impounding crust, the pus escaped, and septic absorption had ceased for good.

Stories of this sort I could multiply indefinitely. The moral of them all is that although tertian and quartan periodicity are absolutely pathognomonic of malaria, quotidian periodicity is of no value whatever as a diagnostic sign for or against this infection.

A useful hint is sometimes got from the particular period of the day at which the individual ague-like paroxysms or rises of temperature commence. A malarial paroxysm may come on at any hour of the day or night, very often during the forenoon. The fever attending septic processes commences almost invariably in the late afternoon. There is ground, therefore, for the presumption that a quotidian fever setting in before noon is malarial.

There is another point to be borne in mind in the diagnosis of febrile disease in patients from the tropics. Sometimes in cases in which malaria complicates septic disease, as for example breaking down tubercular lung, we are apt to be misled by the dominating symptoms attending the well-marked local disease into overlooking the concurrent malarial complication. If in any such case the fever begins early in the day we are to suspect and examine for a superposed malarial infection. Something of the same sort is not at all uncommon in typhoid in the tropics. Therefore, whenever in phthisical or in typhoid patients from the tropics eccentric rises of temperature occur early in the day the patient should be tested for malaria, especially so if there is marked splenic enlargement.

Sometimes in the course of a typhoid we get intercurrent attacks of malarial fever, and not infrequently the oncoming of typhoid in malarial subjects is heralded by an acute malarial manifestation. Be careful about prog-

nosis in such cases. Do not jump to the conclusion that if you remove the malarial element you will cure the patient.

No diagnosis of malaria can be said to be complete unless confirmed by a microscopical examination of the blood. In all cases of doubt such an examination must be made. In undertaking this, and in acting on the result of such an examination, do not forget that a negative result in the case of a patient who is taking, or who has recently taken, quinine is valueless. Even a small dose of quinine, three or four grains, although insufficient perhaps to cure the disease, may be quite sufficient to ruin the blood for microscopical diagnosis. Therefore inquire of any patient whose blood you propose to examine for malaria as to whether he has taken quinine recently or not.

To the expert the recognition of the malarial parasite is an easy matter, but to those unpractised in this kind of work the examination of the blood for malaria is not only difficult but it is unreliable. There are so many possible fallacies that it is only after much practice that one is able surely to recognise them all. Blood platelets superposed or underlying corpuscles, vacuoles, specks of dirt, crenated or buckled corpuscles, even normal physiological blood elements may be readily mistaken for parasites. The inexperienced should never undertake responsible diagnosis on microscopical grounds alone. If not absolutely sure of himself he should either disregard his results and trust rather to the history of the case, to clinical symptoms and the effects of quinine, or he should get his slides examined for him by an expert. And in judging of the capacity of anyone who claims to be an expert do not let the possession of a microscope with a

high-power immersion lens be the only guarantee that the owner is capable of making a proper blood examination. There are more mistakes made in the diagnosis of malaria with the microscope than perhaps over any other similar study; on the other hand, if properly employed, it may give invaluable information leading perhaps to the saving of life.

Although it is not everyone who can make a reliable examination of the blood in malaria, certainly everyone can make a blood film suitable for such a purpose. Every physician in these times should carry in his hand-bag a box of microscope slips. At any time he may be called on to examine the blood, not only for the diagnosis of malaria, but also for the diagnosis of other diseases. He should be prepared for this.

In my experience the best and easiest way of preparing a blood film for the detection of the malaria parasite is to spread the blood on a carefully cleansed slip—not on a cover glass. Proceed thus:—Clean the patient's finger; prick the finger pad with a clean medium-sized needle; express a droplet of blood about the size of a pin's head; touch this lightly with the face of the slip—rather towards one end of the latter, taking up only a very small quantity of blood; lay the shaft of the needle on the blood at right angles to the length of the slip; pause a moment until the blood has run out between the needle and slip, and then push or draw the needle over the surface of the glass. A very delicate film is thus obtained. Three or four such preparations should be made. They should be allowed to dry in the air and then be carefully stowed away in a dustless box, or wrapped in clean paper and sent to the laboratory. Of course fresh wet blood films could be examined; but this neces-

sitates a microscope at the bedside, and it is not always convenient to carry so bulky and heavy an instrument about with one. The stained dry blood films give equally, or even more, reliable results.

In my opinion the best stain for practical work for the detection of the malarial parasite is Leishman's modification of the Romanowsky method. Five or six minutes suffice to fix and stain the blood film, and in a moderate infection there is no difficulty in finding the parasite almost at once. The search may have to be prolonged to a quarter or even half an hour before a negative result can be definitely pronounced upon.

I could relate many cases illustrating the value of the systematic use of the microscope in the diagnosis of malaria, and the danger of neglecting it; I must content myself with two.

About three years ago I was asked to see a young man who had just been brought to London from abroad where, for some time, he had been confined in a lunatic asylum. He was quite off his head when I saw him. The story I got from his father, who had brought him to England, was that the lad had been a planter. He had been in the habit of writing to his parents regularly every week. Several weeks having elapsed without the usual letter, the parents became anxious and telegraphed for information. The reply to this being unsatisfactory the father and mother, suspecting something wrong, set out for the place where their son had been employed. On arriving there they were informed that he had been taken to a lunatic asylum. There they found him in a semi-demented condition. They were allowed to remove him, and accordingly brought him home. The account I got of the illness was by no means a lucid one. I

noticed, however, the extremely anæmic condition of the patient, and on making a physical examination discovered that his spleen was enlarged. Blood films revealed enormous numbers of malarial crescents. Under treatment the lad slowly improved, but I am not quite sure if his mental faculties were ever completely restored. Had a microscopical examination of this lad's blood been made soon after he fell sick he would have been spared the lunatic asylum, a long illness, and the risk of permanent damage to his intellect.

Last winter, I saw in the country, in consultation, a young military officer just returned from India. The suggestion given me was that he might be suffering from acute yellow atrophy of the liver. The history was of military service in Somaliland and latterly on the Afghan Frontier. He started for England on furlough leave in excellent health, but on the railway journey to Bombay he got an attack of what was regarded as jaundice. When he got on board the steamer at Bombay he must have been seriously ill, for he was confined to his bunk for upwards of a week. Towards the end of the voyage he improved and was able to be on deck; and when he arrived in England on a Sunday, although he complained of headache and had a jaundiced appearance, he was sufficiently well to be able to mix with the other members of his family. On Monday the headache was worse and he took to bed; on Tuesday the doctor was sent for. There was now a temperature of 102° F. and jaundice was marked. On Wednesday he was slightly delirious: on Thursday he was completely off his head. He complained of intense headache and of great weakness, and had a certain amount of fever. I saw him on Friday morning. He looked very ill. His expression was vacant

and staring; his pupils were dilated; his head was retracted. The temperature in the axilla was about 102° F., but he was so universally hyperæsthetic that it was impossible to move him so as to make a satisfactory physical examination. An attempt to turn him on his side so as to permit of an examination of the bases of his lungs caused acute suffering. He shrieked with pain and was thrown into a condition approaching opisthotonos. I succeeded in ascertaining that the hepatic area was of about normal dimensions; I also found that the spleen was slightly yet definitely enlarged. The case I regarded as one of cerebro-spinal meningitis, and accordingly gave a very gloomy prognosis. After I left the house an eminent nerve specialist was sent for. He confirmed my diagnosis and prescribed a serum therapy. Meanwhile I returned to London and examined the blood films which I had prepared at the time of my visit. Judge of my astonishment to find them full of malignant malarial parasites, including many crescents. I telegraphed at once to the patient's medical attendant what I had found, reversing my prognosis and prescribing large and repeated hypodermic injections of quinine. Within a few hours of commencing this treatment the symptoms improved, and in a very short time the patient was convalescent. When I last saw him he was quite well.

This was a pernicious cerebro-malarial attack simulating meningitis. But for the blood examination the patient would almost certainly have perished, and doubtless the cause of his death would have been registered cerebro-spinal meningitis.

These cases and many a similar lesson have impressed on me the extreme value of blood examinations in the diagnosis of disease, especially of tropical disease. I

regard the microscope as even more indispensable in this department of practice than the stethoscope or any other diagnostic appliance.

I have already alluded to the value of quinine as a diagnostic in malaria. Personally, I have never seen a malarial fever which has altogether resisted the proper use of quinine, provided the case has not already passed into a hopeless condition. Quinine, therefore, is not only of value in treatment, but also for diagnosis. Any fever which persists unmodified after forty-eight hours' dosing with quinine, is not a malarial fever.

It is important, however, that the dose be adequate, that it be properly administered, and that the drug be absorbed. Ten grains of quinine, repeated two or three times, I regard as an adequate dose. For a responsible diagnosis it should be given in solution. Never trust, either for diagnosis or for treatment, to quinine in tabloid or in pill form. Over and over again I have seen not only errors in diagnosis but very grave results accrue from the administration of quinine in this way. In acute malaria the mucous surfaces, especially of the stomach and bowel, are almost invariably in a catarrhal condition and do not readily dissolve or absorb drugs. Pills and tabloids in such circumstances often pass through the alimentary canal undissolved.

Again, if a patient is vomiting it is hopeless to expect a definite therapeutical result from any drug administered by the mouth.

Therefore in giving quinine by the mouth for diagnostic purposes, give it in solution or, if the patient is vomiting, give it hypodermically. Otherwise you have no assurance that the therapeutic test has been properly applied.

To sum up, I feel justified in saying that no disease is more certainly recognisable than malaria, provided we set about the diagnosis in the proper way and employ intelligently one or all of the tests at our disposal—periodicity, microscopical examination of the blood, and quinine. There are subsidiary marks of this infection, such as enlargement of the spleen; but as they occur in other diseases as well as in malaria they cannot be regarded as of serious value in difficult cases, and in such circumstances should, like quotidian periodicity, be wholly disregarded.

VIII.

The Diagnosis of Tropical Fevers—(*continued.*)

We have to deal with a case of long-standing, or of frequently-recurring fever. The patient has come from the tropics or some warm country. By a careful and systematic examination of the organs from head to foot we have excluded suppuration. Tuberculosis and syphilis have also been dismissed. We have applied the diagnostic tests described in my last lecture, and we have definitely excluded malaria. Which of the remaining seven of the eight tropical diseases that I enumerated as being associated with chronic fever may our patient be suffering from:—Mediterranean Fever, Liver Abscess, Elephantoid Fever, Trypanosoma Fever, Tropical Splenomegaly, Relapsing Fever, or Leprosy?

I shall take these diseases in the order of frequency which, judging from my own experience, they crop up in tropical practice in temperate climates.

Mediterranean Fever.

This is one of the many names applied to the disease produced by the *Micrococcus melitensis*. It is also known as Malta Fever, Rock Fever, Febris undulans, and by many other names. It occurs especially in the countries and islands of the Mediterranean, more espe-

cially in Malta. Apparently it is to be reckoned with occasionally in other warm countries, for cases have been reported from India, the Philippines, the West Indies, and it may be elsewhere, even in countries which cannot claim to be regarded as tropical or even warm. I have seen two cases, and have heard of others, which originated in England and which, with a reasonable amount of certainty, could be traced to infection from imported cases or to fomites.

The disease usually begins, like an enteric, with prostration, headache, furred tongue, anorexia and slow ladder-like rise of temperature to 103° Fahr. or thereby. The fever continues for about a week or longer, and then slowly subsides in the same ladder-like way that it commenced. After a week or two weeks, or even longer, of absolute apyrexia, or it may be only of relative apyrexia, the fever recurs, persists for a variable time, and then once more subsides. And so on, wave of fever following wave of fever for many weeks, or many months even, and until the patient has lost all confidence in the physician and the physician is heartily tired of the patient.

This is the most typical form of Mediterranean fever; but it is far from being the invariable form. There are cases in which the elevation of temperature is maintained continuously for months; others in which the temperature oscillates up and down daily like a quotidian malarial attack; and there are others again which, in their febrile manifestations, are a sort of combination of the foregoing types, exhibiting extreme irregularity in their temperature curves. Thus we have an undulant type, a continued type, an intermittent type, and a mixed type of Mediterranean fever.

During the progress of the disease the spleen enlarges, and may in certain instances become quite palpable. The patient becomes emaciated, anæmic, and sometimes very prostrate. In almost every instance he is the subject of rheumatic-like pains in one or more joints, ligaments, or fasciæ; and very often, especially towards the end of the disease, he suffers badly from sciatica or other form of neuritis. In a proportion of cases orchitis occurs. The rheumatic and neuritic affections exhibit a marked tendency to sudden metastasis, and may be present, and even severe, during the intervals of apyrexia, and also persist when all other symptoms of the disease have subsided.

In addition to being tortured with these pains the patient at one time or another during the progress of his illness is subject to profuse nocturnal sweats. So profuse are these sweats that he may have to change his garments three or four times in the course of the night.

There may also be a tendency to bronchitis, to congestion of the bases of the lungs, to constipation.

Cases vary much in severity. Some suffer from little more than malaise; others are profoundly prostrated and in imminent danger of their lives. On the whole, as regards danger to life, the disease is not a serious one. The case mortality is low, something like two or three per cent., death being brought about by suddenly-developed hyperpyrexia, or by pneumonia, by asthenia, or by some intercurrent disease.

But although of little gravity as regards the attendant mortality, Malta fever is a serious malady to the British garrisons and fleets in the Mediterranean. In Malta especially a large proportion of the men are annually

attacked, and in consequence of the prolonged nature of the disease it has become a positive tax on British interests in that part of the world.

Diagnosis principally hinges on the exclusion of malaria, typhoid, tuberculosis, syphilis, liver abscess, and other forms of suppuration; the recurring or undulant character of the prolonged fever; the presence of rheumatic-like and neuritic pains; the profuse nocturnal sweats; and the locality in which the disease was acquired. A fever, then, of the type described, which is not malarial, is not typhoid, tuberculosis, syphilis, liver abscess, or symptomatic of other form of suppuration, and which originated in the Mediterranean basin, more especially in Malta, may, for all practical purposes of diagnosis and treatment, be assumed to be Mediterranean fever.

It is unfortunate that we have no readily available diagnostic indication in this disease, such as the microscope supplies in malaria, and the skin eruption in the exanthematous fevers. Diagnosis has to rest principally on negative evidence and a balancing of probabilities.

Lately a serum test has been extensively employed in the diagnosis of Mediterranean fever. Under ideal conditions, such as you may get in hospitals in which these cases are common and where reliable cultures of *Micrococcus melitensis* are obtainable, the serum diagnosis may be of real value; but under ordinary conditions of general practice, and with the cultures to be found in ordinary laboratories, my experience is that for diagnostic purposes the serum reaction is thoroughly unreliable. Apparently *Micrococcus melitensis* in some circumstances quickly loses its agglutinating characters and in other circumstances may react to serums other than those from Malta fever patients.

When it was first brought out I used this test. Several unpleasant experiences have led me to discard it, unless I am quite sure about the particular culture used and the capacity and experience of the observer employing it.

I was asked to see a gentleman who some months before had been operated on for middle-ear disease. After recovering from the operation he was sent to the Mediterranean to recruit. While there febrile symptoms set in. After a stay of two months in Naples, and getting no better, he was brought home to London. It was then I saw him. I got the history of chronic fever acquired in the Mediterranean. There was no local condition, so far as I could ascertain, to account for the fever; but in consideration of the previous history of middle-ear disease, I thought some recurrence of the old trouble might be at the root of the fever, or I thought he might have contracted Mediterranean fever. Being in doubt, I procured some of his blood and sent it to two clinical laboratories of repute, with a request for diagnosis as to Mediterranean fever and as to typhoid. Next day I got the report from Laboratory "A"—"Malta fever reaction, no typhoid." On the strength of this I gave a favourable prognosis. The following day Laboratory "B" sent its report—"Typhoid fever reaction, no Malta fever." This rather upset the prognosis I was foolish enough to give on the strength of "A's" report. To make sure, I sent another specimen of the blood to Professor Wright of Netley, who introduced and was the first to make use of this serum reaction for the diagnosis of Malta fever. In due course he very courteously replied—"No Malta fever; no typhoid fever."

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Although recognising the theoretical value of the serum reaction in Malta fever, I have ceased for the present to regard it as of practical value to the ordinary practitioner.

Abscess of the Liver.

There are few diseases about the diagnosis of which there is, at the same time, so much difficulty and so much responsibility. I say responsibility; for whereas in the majority of diseases, provided we do not interfere in a meddlesome and foolish way, so far as the interests of the patient are concerned it matters little whether the diagnosis be right or wrong: with a certain number of diseases, inasmuch as a wrong diagnosis may entail a wrong treatment, it is otherwise. To overlook an abscess of the liver, or to treat it as something else, may deprive the unfortunate patient of his only chance of life.

It is inconceivable that severe pain in the right hypochondrium, with definite enlargement and tenderness of the liver, followed by rigors and a long course of hectic temperatures, could be misinterpreted. Such a combination of symptoms compels attention to the liver and forces a correct diagnosis. Unfortunately, in the vast majority of cases, liver abscess is not led up to in this dramatic way. Generally it is a most insidious disease. Occasionally, from first to last, it is almost latent with few and only feebly pronounced symptoms; symptoms which, so far from being thrust upon us, have to be looked for most carefully. Therefore it is that this grave and important disease is so often overlooked by the inexperienced and unwary practitioner. Many times the abscess is discovered only after it has burst through the lung or bowel; even then the nature of the discharge may be misinter-

preted. Sometimes the disease is recognised too late to save life, and only when the important organ concerned has been completely disorganised. Possibly it may be diagnosed for the first time only on the post-mortem table.

After a time, but probably not until several calamitous oversights, the careful tropical practitioner when dealing with obscure cases of disease has always before his mind the possibility of abscess of the liver. This ever-present suspicion is an important clinical asset; bought, it may be, with human life; expensive but precious experience. To suspect the presence of a disease is a first step towards successful diagnosis. Certainly it is generally the first step in the diagnosis of abscess of the liver.

Amongst Europeans in China there are two important diseases which are, or used to be, far from uncommon there. Both of them, usually, in their earlier stages give rise to only feebly marked symptoms. The diseases I refer to are thoracic aneurism, and abscess of the liver. When in practice in China I laid down for my guidance two rules; these I commend to you. One was, that whenever I met a case of non-febrile thoracic trouble which I could not readily diagnose, to suspect aneurism of the aorta and to examine for this. The other was, that whenever I met with a case of febrile abdominal disease which I could not readily diagnose, to suspect abscess of the liver and to examine for this. Those of you who are in the habit of seeing tropical cases should bear these rules in mind; they were the outcome of considerable experience and of a good many mistakes.

Abscess of the liver is a very grave disease. A trouble about it is that this very gravity leads to the feeling that so grave a disease should have its symptoms proportionately pronounced. Unfortunately, too often, the opposite

is the case. In the earlier and more remediable stages the symptoms are generally of a most subdued character. So much so, that the suspicions of the practitioner are not aroused to the gravity of the situation; he does not get soon enough on to the scent, so to speak. Fatal procrastination in instituting a proper treatment may be the consequence.

You are consulted by a patient who tells you he comes from abroad. He may or may not tell you he has fever, meaning malarial fever. He complains of vague feelings of illness; his digestive organs are upset; he has probably lost flesh; he may or may not complain of pain or discomfort in the region of the liver, or it may be in the right shoulder or neck. Mindful of the rule I have laid down, you suspect liver abscess. You go carefully into the history. The first question you ask ought to be, "Have you ever had dysentery?" In nine cases out of ten, as you know, liver abscess is a sequel of dysentery. You will ascertain from your patient that some time before, it may be many months, he did have dysentery. Very likely he will call it diarrhœa, for the attack may not have been of marked severity, or attended with the passage of blood—to the uninitiated the certain sign and only trusted test of dysentery. He may have quite recovered from the bowel trouble, but from that time, or from some subsequent period, very likely supervening on a chill, he will date his loss of health.

You now proceed to make a physical examination. Possibly you have already remarked that in walking or standing he leans somewhat forward, or to the right. On inspection of the exposed chest and abdomen you notice that, although the patient may be somewhat wasted, the epigastrium, instead of being scaphoid, as it usually is

in a thin man, is, on the contrary, somewhat full. You will mark that the movements of respiration are not so free on the right side as on the left, and very probably you observe that there is a certain amount of fulness and perhaps obliteration of the intercostal spaces over the lower part of the axillary and dorsal region of this side. On palpating the abdomen you are struck by the remarkable rigidity of the right rectus muscle; it springs forward as it were, rigid as a board, to meet your fingers, and to shield what surely must be a tender area underneath. Usually the left rectus is not tense. The spleen is not enlarged. The tension of the rectus prevents your palpating the lower edge of the liver, but percussion enables you to ascertain that this organ is enlarged, both upwards and downwards. The enlargement may be either very little or a great deal; cases vary enormously in this respect. Posteriorly there is a corresponding increase of the hepatic area, which may extend almost to the angle of the scapula. Auscultation reveals weak breathing over the lower lobe of the right lung, and it may be friction or a few moist râles. Peritoneal friction over the liver is not uncommon.

Firm pressure in the intercostal spaces over the dull area may elicit an expression of pain; percussion over the epigastrium or along the border of the right ribs is almost sure to do so. Compression of the liver between the hands causes pain or discomfort. A deep inspiration or a cough may cause great pain; as will likewise a sudden jar on the feet as, for example, in coming rapidly downstairs. Shoulder pain I have already mentioned.

You should now insist on the temperature being taken every three hours. If you find that there is an evening rise to 101° or over, and more especially if the patient

informs you that he sweats profusely during sleep, you may be reasonably certain that you are dealing with an abscess of the liver.

Your next step should be to make sure of your diagnosis. Under an anæsthetic explore the liver with an aspirator, having everything in readiness to open the abscess should pus be found. If any localising indication is discoverable, such as local œdema, bulging, or tenderness, insert the needle at that point; but if no such indication as to the site of the pus be discoverable, bear in mind that the favourite seat of abscess in the liver is the upper and back part of the right lobe. To reach this point, and with due regard to the ensuing operation, I would recommend you to thrust your exploring trocar into an interspace in the anterior or mid-axillary line about an inch above the costal border, and to carry it in a direction upwards and backwards, if necessary to a distance of four inches. Do not be afraid; remember that a needle may be thrust into the liver in a line at right angles to the surface of the body to a distance of three or three and a half inches without danger of wounding the large vessels; if the direction be more oblique, the depth to which the needle may be carried with impunity is correspondingly greater. Failing to find pus at one point, do not hesitate to explore in other directions, making at least six punctures before abandoning the attempt. If at a first sitting pus be not struck, do not conclude your diagnosis of abscess is wrong. Symptoms persisting, after a few days try again and again.

With care little danger is to be apprehended from exploratory puncture; on the contrary, it sometimes cures a hepatitis which had not yet gone on to suppuration. It is a deplorable thing to let a patient die of a

[illegible]

[illegible]

[illegible] A [illegible] of size. If the [illegible] has shown [illegible] used to be taught. [illegible] associated with chronic [illegible] may have to be excluded.

When in doubt, however, about any of these diseases, you are justified in making exploratory puncture in the presence of a history of dysentery, evening rises of temperature with night sweats, enlargement of the hepatic area, and tenderness or pain. This combination almost invariably indicates abscess of the liver; it certainly demands exploration.

Abscess of the liver not infrequently discharges through the right lung, the patient coughing up and expectorating large quantities of a characteristic chocolate-coloured, viscid pus. Sometimes in such cases the fever that had puzzled the physician for weeks or months immediately subsides, and the patient rapidly convalesces as the amount of expectorated pus diminishes. On the other hand, the temporary relief may be followed by a recurrence of the fever, such recurrence being usually accompanied by a diminution, or even complete suppression, of the purulent expectoration. After a few days or weeks the expectoration may be renewed and the fever once more subside. This see-saw process may go on indefinitely until the patient dies from exhaustion, or from hæmoptysis, or a successful surgical operation has established an efficient drainage which nature unaided had failed to supply.

It is important to be able to recognise hepatic abscess discharging in this way through the lung. Over and over again I have met with such cases in which the source of the chocolate-coloured expectoration had been completely misapprehended. I have seen the pus sent to the laboratory to be examined for tubercle bacilli; I have seen it, in consequence of a large admixture of blood, diagnosed hæmoptysis from tubercular trouble. A little attention and reflection should obviate such grave errors. The

gummy viscid consistence, and the colour of a considerable proportion, if not of the large proportion of the sputum, are diagnostic. A copius admixture of blood is easily understood if we reflect that the pus comes from a ragged cavity in liver and lung, the softened vascular walls of which readily bleed under the succussion of the harassing cough that is usually present. Once seen and recognised liver pus can hardly be mistaken. The knowledge that liver abscess often discharges in this way, together with an inspection of the discharge, should ensure correct diagnosis.

Tropical Spleno-megaly or Kala-Azar.

The fever associated with Tropical Spleno-megaly, or Kala-Azar, is of the same chronic and irregular type as that of Mediterranean fever. At the outset of the disease it would appear that fever may run high, and for a considerable period be continued or remittent in type. But in the established disease it is mostly quotidian intermittent, rising to 101°, 102° or 103° Fahr. in the late afternoon, and subsiding, often with profuse sweating, during the night to normal or sub-normal. For days, or even for weeks, there may be complete apyrexia; on the other hand, there may be months of an unbroken succession of evening temperatures. Recurrence or exacerbation of the fever is generally easily induced by fatigue, exposure, irregularities in diet, and similar causes. The fever *per se* is not characteristic; but its association with enlargement of the spleen—generally, though not always, very great enlargement—and concurrent enlargement of the liver, in an individual coming from one of the endemic areas, is most suggestive of Kala-Azar, and justifies an

attempt to clinch the conjectural diagnosis by a search for the causal organism—the Leishman body.

Malaria, of course, has already been excluded by the quinine test and by microscopical examination of the blood. The latter has probably indicated the presence of some protozoal infection by the revelation of a leucopenia and a relative increase of the large mononuclear leucocytes.

Before proceeding, whether by splenic or by hepatic puncture, to search for the Leishman body it is important, if such has not already been done, to make a microscopic examination of the blood. Leucocythemia must be excluded; for, should the case be of this nature, wounding of the spleen or liver, no matter how trifling the wound may be, might very well lead to fatal hæmorrhage into the peritoneal cavity.

Leucocythemia having been excluded, puncture of the spleen or, better, as being probably less risky, puncture of the liver may be made with not too big an exploring syringe, or with a stout hypodermic needle. It is not necessary, or desirable, to plunge the needle deeply into the organ selected; and it is not necessary, or desirable, to aspirate a large quantity of blood into the instrument. What is more particularly required is the juice or pulp of the gland, the debris and cells of the organ. The parasite sought for is located principally, if not entirely, in the cells—not in the blood. Although blood may not appear in the syringe on drawing back the piston, most likely there will be a certain amount of gland debris mixed with a trace of blood sucked into the barrel of the needle. Such a sampling of the organ gives the best results. The material thus procured, it may be infinitesimal in amount, should be blown out on to a glass slip, spread in thin

films and allowed to dry. It must then be stained by some modification of the Romanowsky method—I prefer Leishman's—and examined under a twelfth immersion lens. If the Leishman body is present, it is easily recognised by anyone who has seen it before. Its small size, oval contour, relatively large, round or oval, deeply-staining nucleus, and very small, rod-shaped, still more deeply-staining micro-nucleus, serve for its identification. It may be present in vast numbers, isolated, or in groups, and in every field of the microscope; or, especially if much blood has got into the syringe, many fields may have to be searched through before a single example is discovered. The recognition of one parasite suffices to establish the diagnosis.

Before leaving this part of the subject I would utter a word of warning. Puncture of the spleen must not be lightly undertaken. Donovan has recently recorded a considerable proportion of deaths supervening on this proceeding, trifling though it may seem to be. The capsule of the spleen is easily torn by the needle in the rising and falling of the hypertrophied gland during respiration; it is a very vascular organ. The patient and his friends must be informed of the risk, and such precautions as firm bandaging, so as to stop abdominal breathing during puncture, and rest for a time after puncture be enforced.

Trypanosoma Fever.

The diagnosis of the nature of the chronic fever generally, although not invariably, associated with infection by *Trypanosoma gambiense* may be very easy or, owing to the difficulty sometimes experienced in finding the germ, it may be very uncertain.

As already mentioned, it would appear that the African is more resistent to the pyrogenic influence of the parasite than is the European, though usually, even in the African, from time to time a febrile movement is induced.

Just as in Kala-Azar, it would seem that the initial fever, that following immediately on or within a few days of infection, is generally the most severe; and, just as in Kala-Azar, the subsequent fever or fevers may be of the most irregular, diverse, and uncertain character. The spleen may or may not be enlarged; and, if enlarged, it is difficult to determine whether the hypertrophy is attributable to the trypanosoma, or to some concurrent or antecedent malarial infection. At all events the huge spleens and hypertrophied livers, so common in Kala-Azar, are rare in trypanosoma disease.

In the late stages, when the nervous system has become definitely involved, the tremor of the tongue and hands, the physical and mental lethargy, apart from the discovery of the parasite in the blood, make diagnosis comparatively easy; but in the earlier stages of the infection, diagnosis from the clinical symptoms alone may be difficult or impossible.

There are certain symptoms, the concurrence of two or more of which in a case of chronic irregular fever in a European from the endemic area—tropical Africa—are exceedingly suggestive, if not quite diagnostic of trypanosomiasis. These are:—

1. The peculiar erythema described in an earlier lecture. One can hardly overlook the great irregular patches, the broken rings and smudges of cutaneous congestion. Unfortunately, though fairly constant in many, this erythema does not show itself in all cases;

nor is it always present in those cases in which it appears from time to time.

2. The presence of areas of slight or of more pronounced œdema, especially about the face and lower eyelids. Such localised œdemas occur in other parts of the body, but they are specially noticeable in the face.

3. Enlargement of the lymphatic glands, particularly of the cervical glands. These vary in size from that of a pea to almost that of a walnut, and, especially when large, may be painful.

4. Muscular weakness.

5. Tendency to tachycardia.

6. Headache.

7. In the negro—pruritus.

A combination of two or more of these symptoms, but especially of the erythema and the adenitis, with a chronic irregular fever in the circumstances I have mentioned demands a careful examination of the blood and lymph.

In the blood the trypanosoma may be easily found. More generally a long time, hours even, has to be spent in the search before a single specimen is discovered. Sometimes they appear to be almost completely absent from the peripheral circulation. Centrifuging the citrated blood facilitates the search; but, as Greig has pointed out, it is best in feeble infections to search for the trypanosome in lymph procured by puncturing with a hypodermic needle one of the enlarged lymphatic glands. By squeezing and aspirating the gland, sufficient lymph may be sucked or forced into the needle for the purpose. This may be blown on to slides, dried, and appropriately stained. Failure to obtain microscopic evidence in either of these ways suggests, if suspicion be strong, the in-

oculation of rats, mice, monkeys, guinea pigs, or other laboratory animals with a few drops of the suspected blood. If the trypanosome is present it rapidly multiplies, and subsequent microsopic examination of the blood of the test animal will detect them in great profusion.

Elephantoid Fever.

The recurring acute febrile attacks, associated with elephantiasis and most forms of filarial disease, have received the name of "Elephantoid fever." This fever is symptomatic of a lymphangitis which, as a rule, is apparent in the swollen and very painful glands, the long cords of inflamed lymphatics and, most likely, the extensive area of erysipelas-like inflammation of the integuments of scrotum, leg or arm. The inflamed part is already, or is about to become, the seat of elephantiasis or of lymphatic varix. The testes and cords may alone be involved, a condition which has been named, very erroneously, malarial orchitis; malaria has nothing whatever to do with it.

Occasionally, though rarely, it may happen that the inflammation is confined to the abdominal lymphatics, the integuments and superficial lymphatic system entirely escaping. The nature of these rather serious cases is apt to be overlooked. Severe pain in the abdomen, with rigor and high fever in an individual known to be the subject of filarial infection, or who presents such evidences of filarial infection as varicose groin glands, lymph scrotum or chyluria, are highly suggestive of this condition. If a septic fever supervenes on such an attack it probably means lymphatic abscess, and calls for operation. I have seen this in connection with the thoracic lymphatics.

Elephantoid fever is ushered in by well-marked rigor. For a day or two, or even longer, temperature may run high. There is generally severe headache, often vomiting, sometimes delirium. The attack may terminate in crisis of sweating, or in profuse discharge of lymphous material from the inflamed integument. Occasionally abscess forms; this more especially if the scrotum is involved.

As the attacks in some instances recur with an approach to regularity once a fortnight, or once a month, or once every few months, it was believed at one time, especially in India, that the fever had something to do with the lunar cycle; hence it has been called "Moon Fever." More generally, in consequence of the severity of the initial rigor and the profuse terminal diaphoresis, it has been attributed to malaria. Indeed, in Barbadoes, where filarial disease is exceedingly common and malaria of indigenous origin unknown, it is called "Fever and Ague," and regarded and treated as a genuine malarial disease.

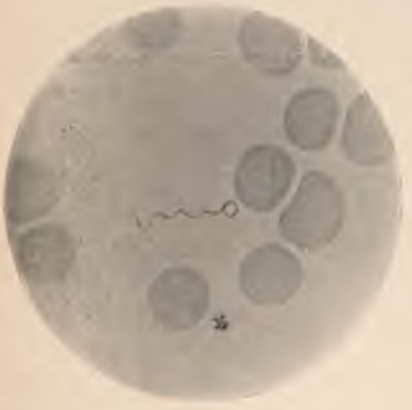
In most cases diagnosis is easy. The implication of some part of the lymphatic system, the history of similar attacks before, the possible presence of the filaria in the blood, and the absence of the diagnostic marks of malaria suffice.

Relapsing Fever.

Some time ago I met in London a case of a recurring fever which had been acquired at Gibraltar. The patient when I saw her was convalescent from one of her fortnightly attacks—the fifth or sixth, I think. As she had been taking quinine in full doses, the case having been originally regarded as malarial, I suggested that the drug

might be stopped, and that I should be supplied with blood films prepared at the commencement of the next fortnightly attack. The fever, as anticipated, recurred after the usual interval, and blood films were sent to me. In every film examined I found a small number of spirilla, or spirochætes, closely resembling *Spirillum obermeieri*. Before the disease finally left her the patient had altogether some eight or nine relapses. Towards the end the relapses gradually diminished in severity.

Manifestly this was a case of spirillar or relapsing fever; but I doubt if it was identical with the ordinary relapsing fever of Europe and India. The large number of relapses is against such a view. I incline to think that the spirillum that produced it is specifically different from that of Obermeier.



Spirillum.
(From a photo by Mr. H. Spitta.)

Recent observations in British East Africa and on the Congo have shown that a spirillar fever, known as "Tick fever," is by no means uncommon in those parts of Africa. As yet, information on the subject is scanty; but it is conceivable that some of these African spirillar fevers are of the same nature as that which I saw from Gibraltar, and recur not two or three times only, as in the European disease, but seven, eight, or more times. If this be so, then it is possible that such cases invalided

home may turn up from time to time in temperate climates, and trouble the conscientious diagnostician.

I would suggest, therefore, that in all cases of fortnightly relapsing fevers from abroad the blood should be examined for spirilla. As it is probable that the parasites would be present only in very small numbers at the advanced stage of the disease likely to be encountered out of the tropics, stained films should be used, and great care and perseverance exercised in the scrutiny.

LEPROTIC FEVER.

I have enumerated a considerable number of chronic tropical fevers; that I have enumerated all I am far from believing. Within the last few years alone, trypanosoma fever and tropical spleno-megaly have been added to the list: I have little doubt that within the next few years yet others will crop up. Keep an open mind in thinking of and dealing with these tropical fevers. Do not commit yourself to a diagnosis when you are not sure about a case; above all, when you are at a loss for a diagnosis don't cloak your ignorance by dubbing it malaria. Be most rigid in your application of the diagnostic canons. If you regard your cases in this way, believing that we do not know everything, and looking for something new, you will discover something new.

Before concluding this part of my subject I would warn you about venturing on a prognosis in any case of chronic fever of which you have failed to recognise the true nature. Especially bear in mind that the skin and nerve manifestations of Leprosy are sometimes preceded for weeks or even months by irregular febrile disturbances. Regard with suspicion all skin lesions and nerve lesions in patients who have at any time resided in the

tropics, more especially if the lesions have been preceded or are accompanied by some vague constitutional febrile disturbance. Test these lesions for evidences of loss of sensation, for associated thickening of the nerve trunks and, in the case of effusion into or thickening of the skin for the lepra bacillus.

IX.

Treatment of Fevers and Fluxes.

Although we may be able to do something to prevent and even to mitigate the suffering entailed by the chronic tropical febrile infections spoken about in my last lecture, it is only over one of them that we possess any real therapeutic power.

Taking them in the inverse order to that in which I have spoken of their diagnosis I propose in this lecture to say a few words about such treatment as we may, with more or less advantage, be able to mete out to them.

Leprotic Fever and Leprosy.

Leprotic Fever and Leprosy, like tubercular fever and tuberculosis, are best met by attempts to improve the general health, as for example by some modification, suitable to the circumstances, of the open-air treatment. If abroad, the patient should return to a cool and salubrious climate and do everything in his power to build up his physiological resistance. Of drugs, Chaulmoogra enjoys the best reputation; that, unfortunately, is not saying much.

Relapsing Fever.

Relapsing Fever calls for the enforcement of those general principles that are applicable to the management of all infectious fevers. There is no special treatment for it.

Elephantoid Fever.

Elephantoid Fever might be attacked with some hope of mitigating the severity of the general symptoms by attention to the local conditions; and by endeavouring to relieve the pain and inflammation of the parts principally affected, by means of fomentations and soothing external applications generally.

Trypanosomiasis.

It is said that trypanosomiasis in man can be influenced by the internal administration of arsenic. Certainly in every instance it cannot be cured by this drug. In at least one form of trypanosoma infection in the lower animals we know that the fever produced by these protozoal organisms, and the reproductive activity of the protozoal organism itself are to a certain extent controlled by the free administration of arsenic. Recent experiments by Laveran and others seem to favour the belief that a combination of arsenical treatment with such drugs as trypanroth, atoxyl, etc., may be even more effectual than that by arsenic alone.

Of course a patient suffering from an infective disease of this nature should be placed under the most favourable hygienic conditions possible; certainly he ought to live in a temperate climate, and not return to the tropics.

The prognosis in trypanosomiasis is undoubtedly grave. Our present knowledge does not permit us to say how grave. I believe a small proportion of the cases do recover.

Tropical Spleno-megaly or Kala-Azar.

The same remarks apply to Tropical Spleno-megaly or Kala-Azar, both as regards treatment and prognosis.

Rogers claims to have obtained benefit from the administration of large doses of quinine. The evidence he has brought forward for this belief is not quite convincing. Quinine, by removing a concurrent malarial infection, may contribute indirectly to the recovery of the case, just in the same way that santonin, thymol, and other anthelmintics may do, but it has no specific action on the Leishman body.

Liver Abscess.

As regards the fever associated with Abscess of the Liver, it is manifest that the only effective treatment is a surgical one. The sooner an abscess of the liver is opened the better chance the patient has of recovery.

It sometimes happens, as I have mentioned, that abscess of the liver discharges through the lungs. In these cases an important practical question crops up. Should such an abscess be opened surgically or should the case be left to itself? Statistics show that of these cases about 50 per cent. recover spontaneously; 50 per cent. die. Can we recognise those that will die and, if so, can we, by interfering in any way, give them a chance of recovery?

Whenever liver abscess ruptures through the lungs, my rule of practice has been to watch carefully the progress of events for ten days or a fortnight. I weigh the patient, keep a careful record of temperature, and measure the daily amount of expectoration. If the fever abates, if the amount of discharge decreases, if the patient gains weight, in other words if things are going well, I recommend that these cases be left alone. But if, on the other hand, the fever does not abate, if from time to time the discharge ceases abruptly and a rise of temperature follows this, and if the patient

gradually loses ground, in such a case I recommend prompt surgical interference as being the only chance of saving life. Do not postpone opening the abscess and thereby establishing adequate surgical drainage; until this is done the case is beset with many dangers. I have seen such a case die suddenly from violent hæmoptysis; I have seen such a case die from abscess of the brain. All manner of intercurrent trouble may occur at any time. Moreover death from exhaustion, if these and similar intercurrent accidents are escaped from, is in the long run inevitable. It is therefore unwise to postpone surgical interference.

It is not my purpose to deal with the surgical treatment of these cases. One word of counsel I would offer, however. Remember the position of the abscess in such circumstances. Necessarily it is in the upper part of the gland. To reach it the needle may have to travel far; and it is quite possible that in such an abscess discharging through the lung, the abscess sac is collapsed, and therefore not easily hit off. Should you fortunately, as you push your needle on into the liver, succeed in lodging it in the abscess cavity, do not remove it. Leave it *in situ* as a guide. After plunging your needle in to its full extent and failing to find evidence of abscess, do not conclude from this that you have not struck the abscess. You may have passed through and beyond it. Therefore in withdrawing the needle, which should be done very slowly, you should be careful to keep a good vacuum, looking out for a sudden appearance of pus in the instrument. On this occurring, immediately stop withdrawal. At that moment your needle is traversing the collapsed abscess cavity. Keep your needle in as a guide, and cut down on it at once.

Mediterranean Fever.

Formerly Mediterranean Fever was treated by low diet and a variety of depressing drugs. The result was that a considerable amount, sometimes a very great amount, of anæmia attended the progress of the fever and retarded convalescence. It used to be the fashion to administer phenacetin, salicylate of soda, quinine, and similar anti-pyretics. Fortunately now-a-days more sensible methods of treatment are in vogue. The patient is not starved or kept on a fluid diet. It is recognised from the outset that the illness may last for weeks or months. Strength is maintained by more liberal dietary, and when he is able to eat it the patient is supplied with such solid food as he feels he can digest.

Of course when the tongue is furred, or headache and fever are present, the appetite is in abeyance. In these conditions a fluid diet of milk, or broth, with fresh lemonade, is advisable; but in the intervals of fever, and frequently in the morning even during the acute febrile stages, the patient can eat well, and then he should be fed well. Beware of monotony in diet; and be careful to include in these cases some form of fresh vegetable food, for scurvy is not unknown as a complication in Mediterranean Fever.

A recent important discovery, bearing more especially on the etiology and prevention of Mediterranean Fever, inasmuch as it may have a bearing or treatment also, I would refer to here.

For some time back a commission of experts, working under the direction of the Royal Society, has been study-

ing this disease in Malta. The commission has accumulated much detailed information; but the most important observation it has published is the fact that a large percentage of the goats in Malta are infected with *Micrococcus melitensis*, and that the milk of the infected goats contains the bacterium. The fresh milk supply of Malta is derived entirely from goats. May not this account for the great prevalence of Mediterranean Fever there and in other places having perhaps a similar milk supply; and, in view of the possibility that it is contaminated with the micrococcus, would it not be wise to withhold, at all events in the endemic area, unboiled goat milk from the dietary of Malta Fever cases?

One thing we should prepare for and be always on the look-out for in Mediterranean Fever, and that is the appearance of hyperpyrexia. A mild case may suddenly assume a very grave aspect. Cold sponging, cold pack, cold bath, the application of cold in various ways should be instantly had recourse to on the temperature getting above 104° Fahr.

If the attack happens to develop in the Mediterranean during the summer, the patient should be invalided to some climate cooler than that of Malta; but if, on the other hand, he is taken ill during the winter, he had better be allowed to remain somewhere in the Mediterranean basin where the climate is more congenial than that of the north of Europe or that of America at this particular season.

Malaria.

There are few diseases of which the management is so simple or so satisfactory as malaria. The treatment practically resolves itself into the administration of one

drug—quinine. Probably we have no remedy in the pharmacopia so nearly deserving the term "specific."

I use the expression "nearly deserving" advisedly, because quinine is not absolutely specific. For the cure of the clinical manifestations of malaria quinine may be relied upon absolutely; but, unfortunately, it cannot be equally depended on for the eradication of the germ of malaria, and therefore for the prevention of relapse.

Quinine has sometimes fallen into disrepute; not because its effect as an anti-malarial drug has been exaggerated, but because either in malarial cases it has been administered improperly, or because it has been administered in cases of disease inaccurately diagnosed malarial. When you fail to cure by quinine a case of supposed malaria it is not the drug that is at fault, it is the diagnosis.

There are several things we must pay attention to in administering this, as in administering other drugs. We must take care that it is given in adequate doses, in a proper form, at the proper time, that its action is maintained during a considerable period, and that, if necessary, its effect should be supplemented or fostered by additional measures.

In an ordinary case of ague from which serious consequences are not to be apprehended—as an ague the result of quartan or of benign tertian infection—my practice is not to aggravate the headache and febrile distress of an existing paroxysm by an immediate administration of the drug, but to wait until the fever begins to break and the sweating stage is well established, and then to give ten grains of quinine in solution. Thereafter I prescribe five grains (also in solution if the patient does not object to the taste) three times a day for a week.

With a view of preventing relapse, fifteen grains should be given every tenth and eleventh day for six months. This treatment is usually absolutely successful. But as in many instances the germ does not die out for some two or three years, I think it desirable to give a short course of quinine, at the spring and the fall of the year, of say fifteen grains every tenth and eleventh day during a month at each of these seasons. I also advise the patient, should he be the victim at any time of exposure or fatigue, or of physiological overstrain, to take one or two fifteen-grain doses of the drug on such occasions.

In severe malarial remittents, especially in first infections, vomiting is usually a prominent symptom. The tongue is foul. It is evident that the stomach is in a highly catarrhal condition. Quinine administered by the mouth at such a time is either immediately rejected or is not absorbed. Nevertheless it is of importance that the patient be brought under the influence of the drug as quickly as possible. If the fever is allowed to run on intense anæmia is rapidly produced, not to mention the possibility of graver dangers. Therefore it is necessary to have recourse to some other method of administering the drug. The best is by hypodermic injection. Seven to ten grains of the acid hydrochloride of quinine in about half a drachm of distilled water should be thrown into some muscular part of the body—preferably into the gluteus muscle. I have never seen quinine administered in this way give rise to the slightest trouble; but I have often seen induration, if not abscess, follow the hypodermic injection of quinine conducted in the ordinary way, which, moreover, is generally exceedingly painful as well as to a certain extent dangerous.

It is of special importance in administering quinine

intramuscularly to observe the strictest asepticism. Solution, syringe and needle should all be carefully sterilised and the patient's skin carefully cleansed and soaked with antiseptic solution.

Before the days of the aseptic idea the hypodermic injection of quinine was not infrequently followed by tetanus; the tetanus, of course, being produced by the tetanus bacillus introduced by a dirty needle or a fouled solution.

These intra-muscular injections of quinine should be continued every six hours so long as the patient cannot retain or absorb the quinine given by mouth. So soon as the stomach settles the drug may be given in the usual way.

Certain grown-up people and all children have an intense objection to the taste of quinine. Fortunately in euquinine, a recently-discovered salt of the alkaloid, we have an absolutely tasteless preparation, one that even children take without a murmur. The dose is the same as for the other salts of quinine.

The tabloid form of quinine is only admissible when the stomach is in a healthy condition. Then tabloids may be trusted if they are not too hard, and if they are easily disintegrated. But in grave cases, particularly in pernicious attacks, we should never expose the patient to the risk of the drug remaining undissolved or not absorbed. Then quinine should be administered intramuscularly, and the dose be large and frequently repeated.

It is the fashion, and I believe a good one, to act on the bowels by some saline purgative from time to time during the progress of a malarial fever, but active purgation is undesirable.

The anæmia following malarial fever is best met by

a combination of arsenic and iron. I find that intra-muscular injections of arsenate of iron act more rapidly than the same drug given by the mouth, and, moreover, if the drug is administered in this form the digestion is not interfered with.

It would be possible to speak at much greater length on the treatment of malarial fevers, but I do not think that any advantage would result from a further discussion of the subject. The beginning and the end of the management of this infection is the administration of quinine. All other drugs are useless in comparison with it. I have tried many of them; I never met with one approaching in efficacy the various preparations of quinine.

Before leaving the subject, I would like to say one word of warning. When a resident of a highly malarious country leaves that country to return to his home in a temperate climate, he is very apt to think that he leaves the tropical disease dangers behind him. Now, the contrary is the case. He carries the disease germs acquired in the dangerous country with him, and only too often they manifest their malignancy when the unfortunate victim thinks he has reached the haven of safety. Often on the voyage home he is attacked by what may prove a fatal fever. It is sometimes said that the bottom of the sea between the West Coast of Africa and England is paved with Englishmen's bones. The moral from this is that the precautions against disease should be continued for months after the subject of infection has left the place in which the disease germ was acquired. I have seen malignant malarial attacks in England five months after the patient had left the West Coast of Africa. Over and over again I have seen Black-water Fever develop many months after the endemic area had been quitted. Therefore, with patients

who have been exposed to malarial influences, a systematic use of quinine should be kept up for at least six months after the patient has ceased to be exposed to the infection.

I had intended to speak at some length on the etiology of the several forms of tropical intestinal flux; but I have used up so much time in discussing the diagnosis and treatment of the recurring and chronic fevers, that I am compelled to confine myself to a very few remarks on the treatment of the two most important of these fluxes, namely, Dysentery and the condition known as Sprue.

You must pardon the egotistical style of the remarks I propose to offer. Lack of time prevents me from speaking of what others think on these subjects, or even of entering into anything like extensive detail on my own views.

In undertaking the treatment of Dysentery it is advisable to endeavour in the first instance to form a mental picture of the condition of the bowel it is proposed to treat. The tendency with many practitioners, especially in this disease, is to disregard almost completely the pathological conditions, and to direct treatment towards checking some leading symptom. Treatment is begun, so to speak, at the wrong end. Bear in mind that a patient suffering from Dysentery is the subject of inflammation—catarrhal, diptheritic, or ulcerative of the mucous membrane of the large intestine. There is, if I may use the expression, a surgical condition at the root of the disease. To treat this surgical condition successfully, the established principles of surgery must be observed and acted on.

And, first, let me remind you that it is against all surgical principles to treat an inflamed or ulcerated surface by blocking up, either by therapeutic or other means, the discharges proceeding from such a surface. To produce constipation, as one sometimes can do by means of opium, in a dysenteric patient, is therefore a thoroughly unsurgical and, in the long run, unsuccessful proceeding. In all cases of intestinal flux I like to regard the intestinal canal in the light of a drainage tube, to be kept open and not on any account to be blocked up. I like to treat a medical disease of this description on what I might call surgical principles—free drainage, rest, and the removal of any specific element that may be present. Rest is an extremely important indication to fulfil, quite as important as drainage. Equally so is the last indication I have mentioned—the removal of the specific element that is certainly present.

In the following remarks I do not wish to be understood as speaking so much of acute dysentery as of the more chronic forms of the disease, although the principles bearing on the treatment are in a great measure identical in both conditions. I wish to speak rather of such dysenteries as you are likely to encounter in patients who have returned from the tropics. You will find that they are all, or nearly all, of the sub-acute or chronic type. In many instances they are amœbic, or, at all events, complicated with the presence of amœbæ in the stools.

The method of treatment which I employ invariably in such cases, unless there is some strong contra-indication, is to insist in the first instance on absolute rest in bed. This measure, even although the disease in some cases is of an insignificant character, should

always be insisted on. It saves time in the long run, and it makes powerfully for success. Then, partly with the idea of fulfilling the same indication, I reduce to a minimum, at all events for a time, the amount of food that the patient receives. I give him just sufficient to keep body and soul together. These two measures—rest in the recumbent position and reduction of the amount of food to a minimum—go a very long way to secure one of the surgical indications to which I have referred.

Then I endeavour to clean the ulcerated or inflamed surface, and for this purpose generally employ a mild aperient, none better than castor oil.

Finally, I proceed to counteract the specific element which I consider is the principal agent in preventing the healing of the inflamed and probably ulcerated surface. If there be not a specific element at the bottom of chronic dysentery, how comes it that the ulcerated surfaces do not heal spontaneously? I believe that in all cases of chronic or relapsing dysentery it is this specific element that is the real cause of the continuation of the disease, just as surely as it is the specific syphilitic germ that prevents the healing of syphilitic lesions, and that until this specific element is removed a healthy healing sore will not result.

And I also believe, and my belief is founded on long experience, that in Ipecacuanha we have a remedy possessing specific powers as against the germ cause of at least certain of the more common forms of dysentery. I regard this drug as belonging to the same category of remedies as quinine, or as mercury, or as salicylic acid. I know that in America and many other parts of the world Ipecacuanha has lost its reputation as an anti-dysenteric. I believe the reason for this has been the inadequate way

in which the drug has been administered. Ipecacuanha should be given in dysentery in exactly the same way as quinine is given in malaria or mercury in syphilis; that is to say, its employment must be kept up for a considerable time. It must be given for many consecutive days—a week, a month, or even longer. I am convinced that used in this way it is a drug of great value and potency; and I would urge American physicians to give it one more trial, at all events in such cases of dysentery as have been acquired in the tropics.

My plan of procedure is as follows:—The patient is put to bed. His bowels are emptied by a small dose of castor oil. He is put on a diet of milk and barley-water, not exceeding in the aggregate three pints in the twenty-four hours. The food is given every two hours from six in the morning until six at night. From 6 p.m. to 9 p.m. he starves. At 9 p.m. he receives a dose of 10 to 15 minims of tincture of opium, and a mustard poultice is applied to his epigastrium. At 9.20, just when he is coming under the influence of the opium, he receives 6 five-grain pills of Ipecacuanha freshly made up with a little mucilage. He is instructed neither to eat, drink, speak, or move for at least three hours, and to endeavour to go to sleep. If saliva, as is likely, collects in his mouth, he is directed not to swallow it but to have it wiped away with a towel. Nothing so surely provokes vomiting under these circumstances as the swallowing of the watery saliva that is so often a prelude to emesis. There may be vomiting during the night, but very often, although there is almost always a little nausea, the pills are retained.

Next day the treatment is repeated, only the patient has 5 five-grain pills. On the third day and afterwards

the tincture of opium is omitted and the patient has 4 pills. Next day he has 3 pills; next day 2; next day 1. The five-grain dose may be continued for ten days or a fortnight, or, if thought desirable, even longer.

The effect of this treatment is to bring on a certain amount of catharsis, and so surely as this is established the patient will improve. The art in the treatment is to regulate the doses of Ipecacuanha so as to secure a certain amount of catharsis but to avoid the irritation that excessive purging may produce. Very likely when the dose has been reduced to five grains the purging will stop spontaneously, and the patient will then begin to pass healthy motions.

Treatment does not stop here. Most people are apt to assume that because the stool has a healthy appearance the dysenteric ulcer must have healed. This, however, cannot be the case, for these ulcers are often large, an inch or more in diameter, with thickened edges and bases and inflamed periphery. An ulcer of these dimensions and characters, as we know from experience in syphilitic ulceration of the leg for example, requires, even after it has lost its specific characters, several weeks to cicatrise. Therefore I insist on the patient observing the same diet, and the same treatment as regards rest and so forth, for at least three weeks after the motions have become to all appearance quite healthy.

I have tried many other kinds of treatment in chronic dysentery; none of them have proved nearly so successful as that which I have described.

I fully recognise the value of other methods, and especially of the employment of different kinds of injections in the treatment of dysentery. These I regard

as adjuncts to the specific treatment by Ipecacuanha. Many times a lingering diarrhœa, symptomatic of some catarrhal or ulcerated condition of the bowel which has ceased to exhibit specific characters, is checked by judicially timed injections of nitrate of silver or of some other astringent or antiseptic. I constantly use these. There is no more valuable remedy as an auxiliary to the Ipecacuanha treatment of dysentery than castor oil; this, too, I frequently employ. But my mainstay in the management of this disease, as I have mentioned, is Ipecacuanha, and I would like to see the use of this valuable drug revived in this part of the world.

One of the most fatal and, unfortunately, common diseases affecting Europeans in tropical countries, more especially in India, the Malay Archipelago, the Philippines and China, is what is known as Sprue. Manila has a particularly bad reputation for this disease; and doubtless in San Francisco you will see many cases from that part of the world in repatriated Americans.

The nature of this disease is rarely recognised by the practitioner unaccustomed to tropical work. It is usually regarded as an ordinary form of chronic diarrhœa, and is very inefficiently and unsuccessfully treated by a mixed diet, intestinal antiseptics, and astringents.

The importance of the subject is great, for Sprue is one of those diseases which, if improperly treated, nearly always sooner or later terminates fatally; but which, if properly treated at not too advanced a stage, can nearly always be cured.

I believe Sprue to be a disease almost peculiar to the tropics and sub-tropics. I do not know if it has a specific germ cause, but the symptoms and the pathological

conditions are so peculiar, that for all practical purposes it may be regarded as a disease *sui generis* if not specific.

Sprue sometimes commences long—years even—after the patient has returned from abroad; usually, however, the patient returns from abroad in consequence of the disease. He complains principally of three symptoms:

Diarrhœa, usually morning diarrhœa;

Sore mouth;

Abdominal distension.

The stools are peculiar. They are generally loose, often very loose; sometimes of pultaceous consistence; rarely formed. They are nearly always pale or clay-coloured, phenomenally copious and usually fermenting.

The mouth is sometimes better, sometimes worse. When comparatively well the tongue has a remarkably clean appearance, bright red, sometimes appearing as if coated with varnish. At other times the tongue may be slightly or considerably swollen, very red and irritable looking, and dotted with superficial erosions. Similar erosions occur under the tongue, on the inner surface of the cheeks and lips, in the throat, and doubtless in the gullet for the patient often complains of a burning sensation under the sternum, readily provoked by swallowing food. The mouth is so tender that only the blandest substances can be tolerated. Sometimes the tongue is better, sometimes worse, but even at its best the organ is exceedingly sensitive to any sapid food, to wine, or anything but the blandest substances.

The distension of the abdomen is much complained of, particularly after eating.

The symptoms get better and worse; but on the whole in untreated cases emaciation steadily progresses, and

after one or more years of increasing debility and emaciation the patient dies.

On post-mortem examination a condition of bowel similar to that of the mouth may be discovered; that is to say, a congested, eroded mucosa. The wall of the intestine is phenomenally thin, so much so as to be diaphanous. Microscopic section shows destruction of villi and glands, and a sort of fibrotic hypertrophy of the sub-mucous layer.

Success in the treatment of this disease depends on thoroughness, and this implies the intelligent co-operation of the patient. Half measures end almost invariably in disaster. Drugs, unless as palliatives, are of very little, if any use.

The first thing to be done is to convince the patient of the deadly nature of his disease, and exact his promise to carry out faithfully and in the minutest detail the treatment prescribed. This is simple enough, and generally as effective as it is simple. It consists in (1) absolute rest in bed in a warm room and in warm clothing; (2) a diet of milk and nothing but milk, commencing with at most three pints in the twenty-four hours.

The milk should be given in divided doses every two hours, and it must be sipped with a spoon. After every feed the patient should wash the mouth out with some boricated water or other non-irritating antiseptic.

As a rule, within a day or two the patient begins to feel the benefit of the treatment. The irritation of the mouth subsides, abdominal distension vanishes, the motions become solid. The quantity of milk must not be increased until appetite is developed. Then by increments of half a pint at a time the quantity of milk is slowly raised until six pints are consumed in the course

of the day and night. When this amount has been arrived at the patient may be permitted to get up; but exertion and exposure are to be avoided. Additional food must not be permitted until the motions have been quite free from suspicion of diarrhœa for at least six weeks.

The only exception to this rule of an exclusively milk diet is fruit, and of all fruits the strawberry appears to be the best. Indeed, strawberries, and probably other pulpy fruits, appear to have a curative effect on this disease, and may be tried early in the treatment. I have seen strawberries succeed when milk alone has failed.

Occasionally we meet with cases which do not tolerate large quantities of milk. In such cases milk evaporated to one-half its natural bulk may succeed. This certainly should be tried when ordinary milk or peptonised milk fails. Underdone minced meat, given as in the treatment known as the Salisbury treatment, is likewise worth a trial.

Time does not permit me to enter into further detail in the treatment of Sprue. My purpose will be served if I have succeeded in calling your attention to the disease, to its deadly nature, and to the efficacy of a pure milk, or a milk and fruit treatment combined with thorough physiological rest.

X.

Problems in Tropical Medicine.

I propose to devote the major part of this, my concluding lecture, to the statement of some unsolved problems, problems of interest and importance in tropical pathology. It sometimes happens that a mere statement of such problems helps towards their solution.

The first of these has reference to a disease peculiarly, or almost peculiarly, American. I mean yellow fever. It was my intention to speak at some length on the recent remarkable advance in our knowledge of the etiology of this disease; a subject which must ever be of special interest and gratification to Americans, seeing that the more fruitful part of these advances is entirely the work of your fellow countrymen. Time will not permit—what to you is probably quite unnecessary—the recapitulation of the story of the labours of Reed and his coadjutors. I cannot pass on, however, to what I have to say in connection with this work without a word of admiration for the insight, the energy, the skill, the courage, and withal the modesty and simplicity of the leader of that remarkable band of workers. If any man deserved a monument to his memory, it was Reed. If any band of men deserve recognition at the hands of their countrymen, it is Reed's colleagues.

The principal outcome of the labours of these men has been the demonstration, first, that the ultra microscopic germ of yellow fever is present in the blood of the patient during the first three days of the disease. Second, that the first step in the passage of the germ from the sick to the sound is made, under natural conditions, in the stegomyia mosquito. And third, that after about twelve days and upwards in stegomyia the yellow fever germ, when implanted by the said mosquito into another human host, is capable of reproduction, so that at the end of a further period of about three days it has established itself throughout the blood, is causing the violent reaction the clinical manifestations of which we call yellow fever, and is once more in a condition to re-enter the mosquito.

These are great etiological facts. They are of supreme practical and scientific value. Acting on them the United States sanitary authorities expelled yellow fever from Havana. Acting on them they should be able in the future to protect the United States themselves from such terrible epidemic visitations as in the past have swept through some of your cities. They explain much, but they do not explain everything about the yellow fever problem. There is at least one important point on which they do not throw adequate light. It is one which should be grappled with, and if possible settled.

As is well known it is the recent arrivals in the endemic area who are most susceptible to yellow fever infection. They are practically, as regards susceptibility, in the same position as the inhabitants of a town where yellow fever is not endemic, but which from climatic and mosquito conditions is open to occasional epidemic visitations. In the endemic localities the Creole and the

old resident enjoy practical immunity. Why? How has this immunity been acquired? By a mild attack of the disease in childhood, say some. Now if this be the explanation, and if the sanitary authorities have banished yellow fever from Cuba, a generation will grow up there which will be absolutely non-immune as regards the disease. Most surely into this non-immune population virulent yellow fever will be introduced sooner or later, and the end of that island will be worse than the beginning. Then instead of a few non-immune foreigners to prey on the yellow fever germ will have the entire population for its victims, and on that day people will think that it would have been better had Reed never been born.

I cannot think, however, that the immunity of the Creole is to be explained on the hypothesis just suggested, namely, mild attacks of ordinary yellow fever in early childhood. For if this were so, then yellow fever would be practically always in evidence in Cuba and similar endemic localities, and the isolation of a few hundred foreigners by mosquito-net and other anti-mosquito measures could not have sufficed to stamp out the disease, as it certainly has done. There must be some other explanation for Creole immunity.

As a working hypothesis I would suggest that there are two strains of yellow fever virus; one of great virulence, one of little virulence. Specifically the same, they are mutually protective. They differ only in their respective pathogenicity. Some such relationship pertains between them as that between small-pox and vaccinia, or as that between the singularly mild type of small-pox that has prevailed recently in the West India Islands and elsewhere in the Western Hemisphere, and the more familiar and virulent kind of the disease that has scourged

mankind from time immemorial. The native in the endemic area acquires his immunity against the virulent disease from having had the non-virulent disease already.

If this be so the value of Reed's labour will still hold good, and for all time. It would be enhanced could we ascertain, so as to be able to recognize them, the clinical features of non-virulent yellow fever. Or if we could ascertain by what means or process the virus of the virulent disease is robbed of its virulence, or the virus of the non-virulent has its virulence enhanced. I have often speculated, both as regards yellow fever and malaria, as to what may be the effect on the germ by its passage through different species of mosquito, whether one species enhances the virulence, and another species has a contrary effect. The experiments this idea suggests are well worth attempting.

I would suggest therefore as subjects for investigation: First, the clinical marks of non-virulent yellow fever in the Creole in the endemic area of the disease. Second, the influence of species of transmitting mosquito on the virulence of the germs of yellow fever and of malaria.

One of the most important factors in the diffusion of disease is the inter-communication of peoples, whether this be by trade, by travel, by pilgrimages, by wars or otherwise. So long as a community remains isolated and cut off from the rest of the world, so long is it spared many of the diseases of the rest of mankind. Once it begins to rise or be united in any way with the rest of the world, pathological, as well as political, trouble begins. There are various kinds of isolation. Geographical isolation, as by a broad sea or lofty mountain range, for example. In primitive times there

was nothing more effective; but when men began to navigate the seas, and to make roads over or through the hills, the protection afforded by these natural barriers was broken down, and diseases hitherto localised became diffused and almost general. Thus cholera and small-pox, and doubtless many other deadly diseases of the Old World were carried to the New, and to a less extent the diseases of the New World were carried to the Old.

One sometimes wonders, in thinking of the great American disease, yellow fever, why there has not been a similar reciprocity; why this disease has not managed to get itself established in the Eastern Hemisphere. That it is capable of successful exportation has been proved over and over again by epidemics great and small which from time to time have broken out in Europe, more especially in Spain and Italy. Nevertheless yellow fever has not succeeded in establishing itself permanently in that part of the world. Why?

Reed and his colleagues have supplied, partially at least, the answer. The stegomyia mosquito is not a perennial feature in these countries. Apparently the chances of an infected stegomyia bridging the winter season and then successfully inoculating the germ are so small that the disease is killed out for good during the first winter. Yellow fever has managed to establish itself in West Africa, where the conditions are more favourable for its special kind of mosquito.

But, you may say, although yellow fever has been a failure in Europe why has it not succeeded in tropical Asia and its great continent-like islands, countries with teeming populations, stegomyia in abundance (for this mosquito is one of the most widely-diffused and hardiest

of the tropical species), and moreover with a climate in many places almost identical with that of the favourite haunts of yellow fever in America? Why then has yellow fever never appeared there? Why has it never shown itself in the Philippines, for example, or in South China, or in the Eastern Peninsula, in the great Malay Archipelago, or in India, or in East Africa? The answer is an interesting one, particularly so at the present juncture, for I believe this happy state of immunity is about to pass away, or rather is in danger of passing away.

Hitherto there has been little or no active, direct, or rapid communication between the home of yellow fever, tropical America, and these countries. Such trade as there has been has followed along a circuitous route, and any yellow fever germ, whether in man or mosquito, that may have started from Panama, has not succeeded in surviving the long journey. We are now approaching a point in the history of ocean travel and commerce when all this will be changed. In a very few years the Panama Canal will be an accomplished fact. A continual procession of ships will, after traversing the yellow fever area, stream from Panama, and rapidly passing through the warm Pacific Seas, carry freight and passengers to all parts of what is now, as regards the West Indies and Caribbean Sea, the far East, but which then will be the near West. The slow sailing ship managed to carry yellow fever to Europe; well then may the fast-travelling steamer carry yellow fever to Asia. If stepping-stones are needed, there are Honolulu and the Philippines.

This seems to me to be no idle speculation, but a big, ugly fact looming in the near future. It is difficult to imagine the extent of the calamity to Asiatic man-

kind that would follow the successful introduction of an infected stegomyia mosquito into such huge distributing centres as Hong Kong or Singapore. You in America know full well what havoc yellow fever wrought in some of your cities, and that, too, in defiance of all the appliances of civilisation and of the co-operation of an educated sympathetic population. What would happen on the introduction of this disease into a thoroughly non-immune, uneducated, insanitary, superstitious and over-crowded eastern city, into such a place as Canton, or into any of the great centres of population in tropical Asia? The immediate calamity would be terrible in its magnitude, but, even more than this, the East would be permanently contaminated and the traveller and trader in these parts would have another risk and anxiety to face.

We can, with justification, anticipate such a calamity. Can it be prevented? The failure of France to carry through the Panama Canal scheme, and the opportune discovery of the part played by the stegomyia mosquito in the diffusion of yellow fever before America took over the task, look like correlated and providential occurrences.

I believe that a scrupulously-administered quarantine on the Panama Canal, a quarantine which need not be irksome to human beings, but which would be absolutely fatal to stegomyia, would effectually protect Asia against yellow fever. The United States must carry this out. It is one of the responsibilities, of which in my opening lecture I spoke, that your expanding influence has brought you. It is not the least.

These, and other sanitary and medical problems that the construction of the Panama Canal will bring up,

are likely to make that great undertaking historical in the development of tropical medicine. As an engineering work the undertaking is colossal, but so far as I know it involves in this respect no new or important principle; its successful accomplishment, so far as a piece of canal-making goes, is simply a question of money, a mere application of well-known methods and appliances. But from the sanitary point of view it is otherwise. No such gigantic work has ever been carried through in a similar climate. No such opportunity for the application of the new discoveries in tropical pathology has arisen. From this standpoint its progress will be watched with intense interest by all students of tropical medicine. Great Britain has slowly learned by long and life-bought experience how in her tropical possessions and dependencies to maintain the health of her administrators and soldiers, her missionaries, her engineers, and her merchants. This she did long before much was known about the etiology of tropical disease; even before its cardinal principles were apprehended. Her methods were the outcome of experience; hardly of science. The makers of the Panama Canal have a great pull in this respect over the old country; for not only are you the welcome heirs to all this hard-won experience, but you are to-day in a position never until recently enjoyed by Great Britain. About to enter on this undertaking, you are in full possession of that great outstanding etiological fact that most tropical disease is insect borne. I sincerely hope the authorities appreciate this. It is the crux of the situation. It means treasure; it means more than this, it means thousands of human lives; it means success or failure. And when you have made this canal, nay, before and while making this canal, remember

Asia. Do not reciprocate her gifts to you of cholera and plague by a return gift in the form of yellow fever.

I have already hinted at some of the unsolved problems connected with malaria; I will propound another. I do so more especially because it seems to hold out the hope that a little more knowledge—acquirable knowledge—in the direction it indicates might furnish us with an additional weapon in the struggle against this, our ancient foe.

There are certain places in Italy, in India, in Mauritius and probably elsewhere in the malarial zone, in which, although anopheles mosquitoes abound and the surrounding country is highly malarious, malaria of local origin is unknown; islands of health, as it were, set in the middle of an ocean of disease. How comes this to pass? There is a physical cause for it. Can this cause be ascertained? And if ascertained, can it be reproduced elsewhere?

There are two islands in the same sea with practically identical climates. In both culex mosquitoes abound. In both elephantiasis is common. But in one there are no anopheles and no malaria. In the other anopheles is extremely common, and malaria also, as well as elephantiasis everywhere. Why should culex be able to maintain itself in both islands; anopheles only in one? There is a physical cause for the absence of anopheles on the non-malarious island. Is this cause ascertainable, and if ascertained can it be reproduced?

Speaking of culex-conveyed disease, I often wondered when resident in China, and now, knowing more than I did at that time, as to the precise way in which the mosquito transmits filaria. I wonder still more how it

is that any individual in the general population of such countries, and even any American or European visitor, can escape infection. How is it that many of the natives are not literally devoured by these worms? It is true that in some places ten to fifty per cent. of the population harbours the filaria. But in many instances the infection, as judged by the microbes of embryo filariæ in finger blood, is a feeble one, representing probably one or two pairs of parental worms. In other places, though culex may be common enough, the filaria and filarial disease are practically absent. How is it that the filaria, and the diseases it gives rise to, are not in these places infinitely more common?

Imagine a Chinese village in some water-logged rice plain. Mosquitos abound; the air is musical at sundown with their humming. A hundred bites a night is a mild computation of your liabilities should you visit that village. A filaria-charged native comes to live there. Every night he yields his parasites to a hundred mosquitos. In ten days he has infected a thousand of them. They hang about his house; the parasites develop. In due time the mosquitos re-infect him over and over again. They bite his neighbours. They, too, become infected; so that in time one would think every inhabitant in that village must be swarming with filariæ, and that to visit such a place for even one night would mean certain infection.

If you try to infect a mosquito with the filaria, you will find it is one of the easiest and one of the most certain things in experimental pathology. Keep your infected mosquito for some three weeks. When you come to dissect her you will almost surely find several larval filariæ in her proboscis, or in her head, waiting

their chance to he inserted in a human host. And yet under natural conditions, conditions which one would think were eminently favourable to the filaria, the infection is not spread nearly to the extent that supposition and laboratory experience would seem to indicate.

When residing in Amoy, China, if at any time I desired to get a man with filariæ in his blood, I knew that a certain find would be almost any Coolie from a particular district to the north of Amoy, a district called Hooioah. An Amoy-born Coolie was not nearly so certain to yield the worm I wanted. And yet the filaria mosquito is probably just as plentiful in Amoy as it is in Hooioah. How is it that this relative immunity from filaria infection exists in one district and yet is absent from a neighbouring and, so far as mosquitos are concerned, closely similar district? There is a physical reason for the difference. Can this be ascertained and, if ascertained, can it be reproduced?

How is it that a filaria-infected man will go on infecting mosquitos night after night for years; will be bitten by these same filaria-infected mosquitos night after night for years, and yet at the expiration of this time show evidence in his blood of only a mild filarial invasion, and very likely exhibit no sign of filarial disease?

It is easy to propound questions. It is often very hard to answer them. But when the answer involves the discovery of a principle, especially of a principle that can be utilised for the preservation of health, that answer is worth striving for.

One more problem in tropical pathology I would state. It is generally held that elephantiasis arabum, ordinary tropical elephantiasis, is one of the several diseases caused by the filaria. It may be so. I believe it to be so, but I

am bound to confess that the evidence for this belief, though strong, is not absolutely conclusive. There is one important fact that tells against the belief that the filaria is the cause of elephantiasis.

In favour of its filarial origin we might adduce the remarkable coendemicity of disease and parasite. Where the filaria is, there you find elephantiasis. Where the filaria abounds, the South Sea Islands, and most of the West India Islands, for example, there elephantiasis is much in evidence. Where the filaria is absent, elephantiasis is absent; and so far as we know, where tropical elephantiasis is absent, there the filaria does not occur. The filaria is a parasite of the lymphatic system, and in this it gives rise to obstruction of the lymphatic trunks. Elephantiasis is a disease of the lymphatic system, a disease in which there is manifest a lymphatic obstruction. Elephantiasis often supervenes on or accompanies such unquestionably filarial diseases as chyluria, varicose groin glands, lymph scrotum.

These are a few of the points on which the belief in the filarial origin of tropical elephantiasis is based. But, I am bound to confess, their value as evidences for this belief is seriously detracted from by the confounding circumstance that very often, in fact in the vast majority of instances, the filaria is not to be found in the peripheral blood in pure examples of elephantiasias.

If, then, the filaria be the cause of elephantiasis, why is it so commonly absent in the disease? But if the filaria be not the cause of elephantiasis, what have they in common that will explain the remarkable similarity in their pathological manifestations, the passage of unquestionably filarial disease into elephantiasis, and their coendemicity?

My view of tropical elephantiasis is that it is produced by inflammation variously provoked supervening in an area of lymph stasis, the lymph stasis having been brought about originally by filarial obstruction of lymphatic trunks. If this be not the explanation then we have another tropical disease germ to hunt for.

This is another tropical riddle. One that the pathologist of San Francisco might very well grapple with. On the shores of the Pacific, whose island natives are more cursed by elephantiasis and filarial disease than are the inhabitants of any other land, you have abundant material at your hand to work on. You should be further stimulated to undertake this task by the reflection that it is not the natives only of these islands who are the subjects of elephantiasis, but that Europeans and Americans residing there for any length of time are just as liable to acquire the disease. I have seen a good many missionaries and traders from the South Pacific islands with well-marked elephantiasis of a limb or limbs. In not one of them have I found the filaria.

Yet one more problem before I bring these lectures to a close. Tropical medicine, as everyone must admit, has made great advances in recent years. In what way can we best utilise and apply some of this important knowledge so recently acquired? I have strong views on this point—views which I have to express with great diffidence and caution in my own country (in such matters, perhaps, too conservative), but which I have no hesitation in submitting to an American audience.

First: I would have those members of the medical profession who propose to practise in tropical countries thoroughly grounded in tropical pathology, theoretical and applied, before they set about their work.

Second: I would have the rudiments of tropical hygiene suitably taught in all government or other native schools in tropical countries.

Third: I would insist that all government employees in tropical countries should know about and understand the rôle of insects in the spread of tropical diseases. And, further, I would at once discharge an employee who did not adopt those precautions against insect-borne disease that this knowledge clearly indicates.

The first proposition implies the establishment of a school or schools of tropical medicine, either as independent institutions or as annexes to existing medical schools. No better place could be found for such a school in America than San Francisco.

Apart from any consideration in connection with their over-sea possessions, the United States of America have an especial interest in tropical disease. Much of the country lies in the sub-tropic zone; much of it at certain seasons has an almost torrid climate. Tropical plants flourish in your parks and gardens. Depend upon it, where tropical plants flourish, tropical disease germs, if introduced, will flourish also. And, as a matter of fact, we know that they do flourish in this country; malaria, dysentery, yellow fever, ankylostomiasis—to mention but a few of them—are common enough in many parts of the United States.

More than any other city in the Union, San Francisco, although itself enjoying a temperate climate, is especially interested in, and, for that matter, exposed to the importation of tropical and other exotic diseases. Much of the adjacent country is malarious, and, moreover, the thousands of Chinese and Japanese amongst you—continually coming and going, the natives of other

tropical lands visiting San Francisco—natives of the Philippines, of the Hawaiian Islands, of the islands of the South Pacific, people from Central America, from the West Indies, from Mexico, the continual stream of English and other Europeans from the East, and the thousands of repatriated soldiers returning from the Philippines, all conspire to concentrate on this city a larger body of imported tropical and exotic diseases than, in its aggregate and variety, can be found, I believe, in any other city in the world. Some of the disease germs thus so liberally sown will undoubtedly, if they have not done so already, effect a permanent lodgment in this city or in the surrounding country. You have, therefore, a distinct local interest in the subject of tropical diseases.

But over and above this limited, and, if I might call it so, parochial and selfish interest, as one of the great cities of a great country you have in this matter a duty to the nation and to humanity at large. For, if from special opportunities you can forward national interests, it is your duty, as it will be your interest, to recognise and to act on this opportunity. In San Francisco you have a large amount of clinical material on which to draw for teaching purposes—larger, more varied, I am convinced, than could be found in any other city in the United States; you have a body of thoroughly competent teachers, some of whom have had tropical experience; you have already in working order a well-equipped medical school; in fact, you want for nothing except some appropriate organisation and an endowment. I confess to a certain amount of astonishment that the systematic teaching of tropical medicine has not long ago been instituted in San Francisco. Possibly the backwardness in this, in a city in other respects so

advanced and energetic, is to be explained in the light of our experience when some of us undertook the establishment of a school of tropical medicine in London. We met at first much opposition—open and covert. It was pointed out, and pointed out quite correctly, that the principles of medicine that are applicable to the diseases of temperate regions apply equally to those of the tropics, and it was maintained that tropical medicine was already adequately dealt with in the general scheme of medical teachings, and that, therefore, special arrangements for teaching the subject were unnecessary. Most of those who held and acted on this view had themselves never practised in the tropics and had no actual experience of medical requirements there. The arguments they used might be brought forward against any speciality —against opthalmology, against gynæcology, against dermatology, against surgery even, for the principles of pathology are the same for all organs of the body, as well as for all climates. If the argument be valid, there is no necessity for regarding and treating the subjects I mention as departments of our art, demanding special study and special experience for their adequate practice.

But experience has shown that the practical application of the general principles of pathology can best be secured by concentrating study and experience on the particular line of practice circumstances and choice prescribe.

The principles of botany are the same in Manitoba and in Honolulu; but would any prudent investor employ a Manitoba wheat-raiser to grow sugar-cane in Honolulu? Certainly not, unless the Manitoba farmer were previously specially schooled for the work before him. Would the

prudent investor commit his sugar estate into the hands of a professor of Botany even? If he should be so foolish as to do so, I am afraid the dividends would not justify his judgment and choice of a manager.

Special education for special work, when special education can be got, must be got; and more especially is this the case where life and health, the greatest of human interests, are at stake.

To send a young fellow fresh from the schools to some tropical and unhealthy climate to treat diseases he has never seen before, many of which he has probably never even heard of before, is not only cruelty to the doctor, but it may be death to the patients and bad business all around. A merchant would not think of running his business on such lines. Why, then, should the medical business, the most important of all businesses, in that it deals with human life, be run on such lines?

I could cite hundreds of instances in illustration of the folly, I might almost say the criminality, of the old system, by which raw, untaught, and inexperienced youths were launched in tropical practice. Many of these illustrations, I am sorry to have to say, would be culled from the long category of my personal mistakes. But the subject hardly requires illustration; a little reflection will show any thoughtful man who takes medical responsibilities seriously into consideration, how sad, how helpless, the position of a young medical man must be who has had no opportunity of learning something about them, when he is brought face to face with such diseases as cholera, heat stroke, pernicious malaria, liver abscess, leprosy, beri beri, and almost any of the diseases I have been speaking about in these lectures. He will not recognise them, much less treat them successfully. It

is hard for the young doctor, but harder still on the sick man, who has only the doctor's ignorance and common-sense, and the general principles of pathology to fall back on.

Manifestly for such countries as Great Britain and the United States, with vast and extending tropical interests, schools in which tropical medicine can be adequately learned are a necessity.

If demand be any indication of the need of supply, proof of this necessity can be got from our experience in England. Time does not permit me to enter on details, but when I state that within the five or six years since its establishment, over 500 students have passed through the London School of Tropical Medicine, and almost half this number (I think) through the corresponding school in Liverpool, I have no hesitation in saying that the men who leave us are far better equipped for tropical work than those who used to go out to our Colonies direct from the General Medical Schools without special education, or, for that matter, any education in tropical diseases at all. Further than this, I feel justified in saying that many of the recent advances in tropical pathology are owing directly or indirectly to these schools.

We in England borrow many ideas from America; I suggest that, for once in a way, America might borrow an idea—this idea of a tropical school—from us. Our example has been followed in France and in Germany with, I believe, gratifying results. Any prejudice that at its inception may have existed against the London School has disappeared. We are now affiliated to the University of London, and are subsidised by the Colonial Government, the Indian Government, and many of the

Crown Colonies. Our position, therefore, is assured; our schools of tropical medicine have come to stay.

Establish, then, such a school in San Francisco; with your abundant clinical material, your teaching facilities, your unique geographical position, your growing interests in the tropics, it would be bound to succeed.

I have had considerable experience in the working of such an institution. As a result of this experience, I have arrived at certain conclusions affecting constitution and management.

(*a*) The school must be in close association with a hospital where tropical cases are plentiful, or can be concentrated.

(*b*) The laboratory and class rooms should be so near to the wards that the student can have immediate access to any patient whose disease he is engaged in studying.

(*c*) The staff should consist of:—

1. A superintendent demonstrator or tutor, who should have the run of the hospital cases and be director of studies as well as general demonstrator. The salary of this officer must be a good and rising one, so as to secure high ability and, also (and this is of importance), continuity in office.

2. Assistant demonstrators.

3. Lecturers, physicians, and surgeons who themselves have had tropical experience.

(*d*) The length of the course of study should be not less than three months, and the entire time of the student must be devoted to the work.

(*e*) The certificate of the school should be given only to those who have passed a satisfactory examination.

(*f*) There should be special chairs in protozoology and helminthology, subjects inadequately taught in the

medical schools but of great importance in tropical medicine.

(*g*) There should be a research department, a museum, and a library.

(*h*) The school should be open to post graduates only.

(*i*) To meet the convenience and exigencies of medical men returning from or going abroad, and this is a practical point of considerable importance, there should be three complete sessions annually.

(*j*) The superintendent, the protozoologist, and the helminthologist should give their whole time to the school and to research.

At first it might not be necessary to employ so large a staff as I indicate; it might be prudent to begin on a more modest scale. But I would urge you, if you undertake such a school, to lay your plans on a broad basis, so that when expansion becomes necessary—as I fully believe in the near future it would—pulling down and reconstructing, always an expensive proceeding, might not be required.

For the establishment and endowment of such a school, we in London have estimated that £100,000 would suffice. For this wealthy and progressive city, there should be no difficulty in finding such a sum for such a purpose.

Second: As regards the teaching of the rudiments of tropical hygiene to native children, the advisability of, or rather the necessity for such a measure is obvious. Such teaching is eminently practical. It teaches the child how to protect itself from, and how to avoid its most dangerous enemies. It trains its mind to think and to observe. Moreover, when the child by-and-by grows up into a man

or a woman, after such teaching he or she is prepared to accept sanitary measures devised for the general benefit, measures which but for such early education would have been rejected with suspicion or contempt. Sanitary laws are of little use without the co-operation of the masses.

Third: Lastly, I would have all government employees in the tropics, covenanted and uncovenanted, from the governor to the humblest mechanic, aware of and believers in the *rôle* of insects in the spread of tropical diseases.

Government employees are expensive. The Government has a right to protect itself from loss. In the British West African Colonies the official gets twice the salary he would get for doing a double amount of the same kind of work in a healthy climate; and, over and above this, he gets six months' leave of absence for every twelve months' service, besides many other expensive privileges. So that the cost of the administration of these colonies, relatively to their revenues and value, is enormous. And, of course, this cost has a correspondingly retarding effect on the development of the colonies. What is spent on administration cannot be spent on roads, and railways, and other remunerative public works. The unhealthiness of these colonies is the cause of all this. Anyone, therefore, who by carelessness, or from ignorance in this matter of the insect as a carrier of tropical disease germs allows himself to become infected is a dead loss, a very serious loss, but an avoidable loss to the Government of the colony. Such a man is a bad investment. He should never have been employed. Means should be devised to keep such men out of Government service or other public employment. I have no doubt your coming Panama experience will

bear me out in this; I have no doubt your Philippine experience is already bearing me out in this.

I had hoped to speak on this occasion on many other subjects of interest to the student of tropical medicine. I had hoped to say something about plague, about leprosy, about the etiology of dysentery, about many of the other pathological questions of the day as bearing on my subject. But my time is up; my task is finished though not fulfilled. No one knows better than I know how imperfectly, how crudely it has been performed. I trust I have succeeded sometimes in interesting, if not in instructing you. But however that may be, I personally shall always retain a pleasant recollec- of your courtesy and kindness, and of the patience with which you have listened to me.

[719.—11,05.]

(8.50)